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A randomised 2 × 2 trial of community versus hospital pulmonary rehabilitation for chronic obstructive pulmonary disease followed by telephone or conventional follow-up

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Declared competing interests of authors: none

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Abstract

A randomised 2×2 trial of community versus hospital pulmonary rehabilitation for chronic obstructive pulmonary disease followed by telephone or conventional follow-up

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Objectives: To determine whether pulmonary rehabilitation carried out in a community setting is more effective than that carried out in a standard hospital setting and which is more cost-effective; also whether telephone follow-up is both cost-effective and useful in prolonging the beneficial effects of a pulmonary rehabilitation programme.

Design: A randomised trial. Participants were randomised in 2×2 factorial fashion to hospital or community rehabilitation and telephone or standard follow-up with review.

Setting: Hospitals or community sites in Sheffield. The community venues were selected to be close to public transport routes and have good parking and level access. The two hospital venues were the physiotherapy gym and a staff gym within the grounds of the hospital.

Participants: Patients with chronic obstructive pulmonary disease diagnosed by respiratory physicians according to Global Initiative for Chronic Obstructive Lung Disease guidelines.

Interventions: Participants were randomised to one of four groups: hospital rehabilitation with no telephone follow-up; hospital rehabilitation with telephone follow-up; community rehabilitation with no telephone follow-up; or community rehabilitation with telephone follow-up. All were blinded to the telephone intervention arm until 1 month post rehabilitation, when only the assessment team and research participants were unblinded.

Main outcome measures: The primary outcome measure was the difference in improvement in endurance shuttle walking test (ESWT) between hospital and community pulmonary rehabilitation groups post rehabilitation, and the difference in ESWT during 18 months' follow-up between those receiving telephone encouragement and those receiving standard care. A secondary measure was health-related quality of life.

Results: A total of 240 participants had evaluable data. Of these, 129 were randomised to hospital rehabilitation (64 with telephone follow-up and 65 with no telephone follow-up) and 111 to community rehabilitation (55 with telephone follow-up and 56 with no telephone follow-up). For the primary outcome measure, there were 162 patients with data for analysis: hospital rehabilitation with no telephone follow-up ($n=38$); hospital rehabilitation with telephone follow-up ($n=48$); community rehabilitation with no telephone follow-up ($n=43$); and community rehabilitation with telephone follow-up ($n=33$). For the acute phase post-rehabilitation outcomes, before patients had the opportunity for telephone follow-up, we compared outcomes between the 76 patients in the community rehabilitation group and the 86 patients in the hospital rehabilitation group. Patients in the hospital rehabilitation group increased the distance they could walk at the post-rehabilitation follow-up by 283 m (SD 360 m), an increase relative to baseline of 109% (SD 137%). Patients in the community rehabilitation group increased the distance they could walk at the post-rehabilitation follow-up by 216 m (SD 340 m), an increase relative to baseline of 91% (SD 133%). There was no statistically significant difference between the groups [17.8% (95% CI –24.3 to 59.9, $p=0.405$)]. For longer term outcomes at 6, 12 and 18 months post rehabilitation there was no evidence of a rehabilitation group effect. After allowing for the initial post-rehabilitation baseline distance walked, time (follow-up visit) and the factorial design (telephone follow-up group), the average difference in the post-rehabilitation follow-up distance walked on the ESWT between the hospital and community rehabilitation groups was 1.5 m (95% CI –82.1 to 97.2, $p=0.971$), and between the telephone and no-telephone groups it was 56.9 m (95%

CI –25.2 to 139, $p = 0.174$). There was no difference between hospital or community groups in terms of acute effect or persistence of effect. Health economic analysis favoured neither hospital nor community settings, nor did it clearly favour telephone follow-up or routine care.

Conclusions: Pulmonary rehabilitation delivered in a community setting has similar efficacy to that produced in a more traditional hospital-based setting, both settings producing significant improvements in terms of exercise capacity and quality of life acutely and after long-term follow-up. Health economic analysis showed that neither hospital nor community programmes were greatly favoured. The choice of model will depend on local factors of convenience, existing availability of resources and incremental costs. Staff characteristics may be important in gaining optimal outcome, and care should be taken in staff recruitment and training.

Trial registration: Current Controlled Trials ISRCTN86821773.

Contents

List of abbreviations

A&E	accident and emergency department		FEV_1/FVC	ratio of FEV_1 to forced vital capacity (an index of airway obstruction)
ANCOVA	analysis of covariance		FVC	forced vital capacity
ATS	American Thoracic Society		GOLD	Global initiative for Chronic Obstructive Lung Disease
AUC	area under the curve			
BMI	body mass index		HRQoL	health-related quality of life
CEAC	cost-effectiveness acceptability curve		ICH	International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use
CI	confidence interval			
CONSORT	CONsolidated Standards Of Reporting Trials		ISWT	incremental shuttle walking test
COPD	chronic obstructive pulmonary disease		ITT	intention to treat
			LOCF	last observation carried forward
CRQ	Chronic Respiratory Questionnaire		MID	minimum (clinically) important difference
DMEC	Data Monitoring and Ethics Committee		MRC	Medical Research Council
EAC	equivalent annual cost		MUAMA	mid-upper arm muscle area
EQ-5D	an index from the EuroQol		NICE	National Institute for Health and Clinical Excellence
ERS	European Respiratory Society		OLS	ordinary least squares
ESWT	endurance shuttle walking test		PAS	patient administration system
FEV_1	forced expiratory volume in 1 second		QALY	quality-adjusted life-year

continued

RCT	randomised controlled trial		SF-6D	an index from the SF-36
SD	standard deviation		SpO$_2$	oxygen saturation in arterial blood estimated by pulse oximetry
SF-36	Short Form (36 questions) questionnaire			
			TSF	triceps skinfold thickness

All abbreviations that have been used in this report are listed here unless the abbreviation is well known (e.g. NHS), or it has been used only once, or it is a non-standard abbreviation used only in figures/tables/appendices, in which case the abbreviation is defined in the figure legend or in the notes at the end of the table.

Executive summary

Background

Pulmonary rehabilitation is a well-established treatment modality for chronic obstructive pulmonary disease (COPD), recommended in national and international guidelines. The rationale for its use is the observation that breathless people limit their exercise and become cardiovascularly deconditioned, leading to further exercise limitation and a spiral of decline. Exercise training breaks this cycle leading to an improvement in exercise capacity and health-related quality of life, and decreasing breathlessness. Although well supported by research, this has usually been carried out in a hospital environment, and it is clear that the benefit is progressively lost once the course terminates. A programme producing a change in lifestyle is likely to produce more sustained benefits. We hypothesised that a community programme would be seen as more relevant to patients' own lifestyles than a treatment administered in a hospital. However, the converse may be true. People may see community treatment as more trivial than treatment administered in an important hospital. Indeed, one Australian trial, the only other large comparative trial to address this, suggested that community rehabilitation might be less effective.

This trial set out to test this in the context of routine NHS treatment. In addition to effects on exercise capacity and health-related quality of life, we also assessed the health economic impact.

Following a rehabilitation programme, it is unclear whether continued interventions may enhance persistence of effect. We hypothesised that regular telephone encouragement would be cost-effective in encouraging continued exercise and consequent prolongation of benefit.

Objectives

This study sought to establish:

1. Is pulmonary rehabilitation carried out in a community setting more effective than that carried out in a standard hospital setting, immediately or after 18 months of follow-up, as assessed by exercise capacity and indices of health-related quality of life?
2. Is telephone follow-up useful in prolonging the beneficial effects of a pulmonary rehabilitation programme?
3. What is the most cost-effective choice for the setting of pulmonary rehabilitation, and is telephone follow-up a cost-effective option?

Methods

Patients with COPD diagnosed by respiratory physicians according to Global Initiative for Chronic Obstructive Lung Disease guidelines were randomised to receive rehabilitation in a hospital or community setting. Treatment was in a group setting, twice per week for 6 weeks, according to a standardised protocol. Hospital and community groups were supervised by the same team. Research participants were also randomised in 2×2 factorial fashion to hospital or community rehabilitation and telephone or standard follow-up with review. Exercise capacity, generic and disease-specific quality of life, and health economic data were collected pre and post rehabilitation, and at 6, 12 and 18 months following rehabilitation.

Results

A total of 240 participants had evaluable data. Of these, 129 were randomised to hospital rehabilitation (64 with telephone follow-up and 65 with no telephone follow-up) and 111 to community rehabilitation (55 with telephone follow-up and 56 with no telephone follow-up). For the primary outcome measure, there were 162 patients with data for analysis: hospital rehabilitation with no telephone follow-up ($n = 38$); hospital rehabilitation with telephone follow-up ($n = 48$); community rehabilitation with no telephone follow-up ($n = 43$); and community rehabilitation with telephone follow-up ($n = 33$). For the acute phase post-rehabilitation outcomes, before patients had the opportunity for telephone follow-up, we compared outcomes between the 76

patients in the community rehabilitation group and the 86 patients in the hospital rehabilitation group.

The primary efficacy response variable was the percentage change relative to baseline, i.e. [(end of rehabilitation−baseline)/baseline] × 100, in distance walked during the endurance shuttle walking test (ESWT), as specified in the protocol. Patients in the hospital rehabilitation group increased the distance they could walk at the post-rehabilitation follow-up by 283 m [standard deviation (SD) 360 m], an increase relative to baseline of 109% (SD 137%). Patients in the community rehabilitation group increased the distance they could walk at the post-rehabilitation follow-up by 216 m (SD 340 m), an increase relative to baseline of 91% (SD 133%). There was no significant difference in improvement between the groups, mean difference in the change in distance walked was 17.8% (95% CI −24.3 to 59.9, p = 0.405, n = 161) in favour of hospital rehabilitation.

For longer term outcomes at 6, 12 and 18 months post rehabilitation there was no evidence of a rehabilitation group effect. After allowing for the initial post-rehabilitation baseline distance walked, time (follow-up visit) and the factorial design (telephone follow-up group), the average difference in the post-rehabilitation follow-up distance walked on the ESWT between the hospital and community rehabilitation groups was 1.5 m (95% CI −82.1 to 97.2, p = 0.971). There was also no evidence of a telephone follow-up group effect. After allowing for the initial post-rehabilitation baseline distance walked, time (follow-up visit) and the factorial design (rehabilitation group), the average difference in the post-rehabilitation follow-up distance walked on the ESWT between the telephone and no-telephone groups was 56.9 m (95% CI −25.2 to 139, p = 0.174). The high attrition rate during follow-up gives rise to some uncertainty in these results, although data imputation does not suggest that important differences were concealed by differential dropout.

The pulmonary rehabilitation programme used was shown to produce clinically important benefits in exercise capacity and health-related quality of life acutely. This declined as expected during follow-up. There was no difference between hospital or community groups in terms of acute effect or persistence of effect. Telephone follow-up did not significantly alter maintenance of exercise capacity or generic quality of life indices. Although disease-specific quality of life assessed by the Chronic Respiratory Questionnaire was statistically significantly better maintained after telephone

follow-up than after standard care, the mean effect was small and below the accepted minimum important difference. Health economic analysis favoured neither hospital nor community settings, and nor did it clearly favour telephone follow-up or routine care.

Exploratory post hoc analysis suggested that the team delivering the care could have a large effect on magnitude of improvement. A significant proportion of those apparently suitable for rehabilitation and agreeing to it dropped out before commencing the programme.

Conclusions

Implications for health care

- Pulmonary rehabilitation delivered in a community setting has similar efficacy to that produced in a more traditional hospital-based setting, both settings producing significant improvements in terms of exercise capacity and quality of life acutely and after long-term follow-up.
- Telephone follow-up versus standard care showed no difference in exercise capacity or generic measures of health-related quality of life. There was however a small improvement in disease-specific quality of life in the telephone follow-up group. Although statistically significant, the mean effect was below the minimum important difference.
- Health economic analysis showed that neither hospital nor community programmes were greatly favoured. The choice to adopt either model will depend on local factors of convenience, existing availability of resources and incremental costs.
- Planning of service delivery needs to acknowledge that uptake of pulmonary rehabilitation by those who might potentially benefit will be incomplete. Measures to enhance this (e.g. transport provision and convenience) have the potential to have major public health impact.
- Our data suggest that staff characteristics may be important in gaining optimal outcome. Care should be taken in staff recruitment and training.

Implications for research

- There is a clear need for further research to identify ways of enhancing uptake of pulmonary rehabilitation programmes by those with potential to benefit from them.

This needs to include detailed qualitative research to identify patient-centred strengths and weaknesses in such standard models of pulmonary rehabilitation.

- Further research is required into the efficacy and safety of community rehabilitation programmes in important patient groups not covered by this study, in particular those receiving long-term oxygen therapy and those with cardiac failure.
- Initial maximal exercise testing was carried out in a hospital setting. Further research is required into the safety of such maximal testing in community settings.
- Our exploratory analyses suggest that the magnitude of benefit of a pulmonary rehabilitation programme may be significantly affected by the team supervising this intervention, and admits the possibility that such an effect could be large. This merits further specific research.
- Telephone follow-up using a very simple model produced some improvement in long-term disease-specific indices of health-related quality of life. Research is required to test whether more complex telephone follow-up models could produce further benefit, and to test the cost benefit of any such approach.

Trial registration

This trial is registered as ISRCTN86821773.

Chapter 1
Introduction

Background to the study

Chronic obstructive pulmonary disease (COPD) is a common condition imposing significant burdens on large numbers of patients, with important implications for health-care providers from a clinical and cost point of view.[1] Pulmonary damage is largely irreversible so pharmacological treatment is necessarily limited in its efficacy. As a consequence of breathlessness, people with COPD tend to limit their exercise and become deconditioned. It is now firmly established that a pulmonary rehabilitation programme of structured exercise (usually accompanied by an educative programme) yields significant health benefits. A Cochrane Review concluded in 2006 that 'Rehabilitation relieves dyspnoea and fatigue, improves emotional function and enhances patients' sense of control over their condition. These improvements are moderately large and clinically significant.'[2]

Early studies of pulmonary rehabilitation sometimes involved very intensive programmes, for instance a Canadian study used an 8-week inpatient programme followed by a 16-week supervised outpatient programme.[3] Subsequent trials have taken place in a variety of settings: hospital inpatient, hospital outpatient and community. The term 'community' may refer to group rehabilitation of a similar nature to that carried out in a hospital, but it is also used to describe home care, with one-to-one supervised exercise. Home rehabilitation may well be useful for very disabled patients who are unable to access services outside the home, but it is likely to be labour intensive and expensive, limiting its utility to a minority of those with significant impairment. Here we use the term 'community rehabilitation' to refer to supervised group rehabilitation in non-hospital venues.

Although there are undoubtedly great beneficial acute effects of pulmonary rehabilitation, these unfortunately decline at the end of the rehabilitation period.[4,5] The American Thoracic Society (ATS)/European Respiratory Society (ERS) statement on pulmonary rehabilitation notes that: 'Pulmonary rehabilitation is a service that complies with the general definition of rehabilitation and achieves its therapeutic aims through a permanent alteration of lifestyle.'[6] We and others wondered whether community rehabilitation would not only enhance adherence to exercise programmes by facilitating ease and convenience of participation, but also enhance its efficacy by linking it effectively to a lifestyle change rather than being a treatment that others apply in a hospital.[7,8]

This theme of moving services to community settings where possible has been adopted as official policy in the UK.[9] Community programmes have begun to be increasingly established. A cautionary note is sounded by the ATS/ERS joint statement: 'Properly conducted pulmonary rehabilitation offers clinical benefit in all settings that have so far been studied; however, few clinical trials offer direct comparison among various settings. The majority of studies describing the benefits of pulmonary rehabilitation are derived from hospital-based outpatient programs.' In assessing the evidence base for community programmes, the National Institute for Health and Clinical Excellence (NICE) guidelines conclude, 'The majority of studies have been performed in a hospital setting. There is limited data on effectiveness in community or home studies and there have been no comparative studies.'[1]

Aims of the study

It seemed timely therefore to examine further the evidence for the efficacy of pulmonary rehabilitation in a community setting acutely as well as chronically, and to compare the efficacy with that of a more traditional hospital-based approach.

As noted, the benefits of treatment decline with time after pulmonary rehabilitation has finished. This has led to a search for ways to prolong its benefit, including such intensive strategies as repeated courses of rehabilitation[10] and weekly supervised rehabilitation.[11] Whilst these have shown promise, they are expensive and no data have been advanced to explore the cost-effectiveness of such approaches.

As we hypothesised that effecting a lifestyle change was key to producing lasting benefit, we wondered whether simple telephone encouragement without direct health-care contact would be beneficial.

From a UK perspective it was important to have a trial that examined service delivery within the NHS. As models of health-care delivery vary widely in other countries and hence will lead to different preconceptions and expectations, it is not certain that models examined elsewhere can be generalised to the UK system.

This study therefore undertook a 2×2 factorial trial of:

- pulmonary rehabilitation in hospital or community settings
- telephone follow-up or 'standard follow-up'.

Acute effects of rehabilitation together with 18-month follow-up are included, with data on exercise capacity [using the endurance shuttle walking test (ESWT)] and quality of life (using generic and disease-specific tools). Cost–benefit analysis is also included.

Research question

At the first meeting with the Data Monitoring and Ethics Committee (DMEC) it was agreed that clarification of the hypothesis was indicated, particularly in relation to the specification of co-primary outcomes, and indeed the effect of this on the power calculation. It was noted that whilst there were data to enable the power calculation in relation to the initial changes in walking distance, it was not possible to predict the statistical variation relating to follow-up, and thus this aspect of the study should be excluded from the power calculation.

The redrafted hypotheses underlying the study were agreed and are:

1. The percentage change in the endurance shuttle walk post rehabilitation, compared with the baseline measurement, will be greater in the community-based than in the hospital-based group.
2a. Community-based rehabilitation will increase the persistence of the changes observed in hypothesis 1.
2b. Telephone follow-up will increase the persistence of the changes observed in hypothesis 1.

Chapter 2
Methods

Changes to original protocol

Prior to the study we suggested that leisure centres be used for community rehabilitation, which would allow research participants to continue with programmes. This proved impossible as we had little co-operation from suitable leisure centres, and there was limited availability for continuation programmes on a city-wide basis.

In an ongoing community pulmonary rehabilitation programme in one suburb of Sheffield it had been possible to arrange transport with a voluntary body on a regular basis. This proved impossible to organise for our multicentre requirements, so we provided introductions to the voluntary body or provided personalised transport information if necessary from the local bus company. We felt that this was appropriate in view of the pragmatic nature of the intervention.

The self-completion version of the Chronic Respiratory Questionnaire (CRQ) was withdrawn immediately prior to the study, necessitating creation of our own self-completion version for all follow-up visits. The original interviewer-led questionnaire was used at visit 1, which is when subjects choose five items causing breathlessness that are most important to themselves. These items are then used in one section of the questionnaire at follow-up visits. The self-completed version (Appendix 2) adds a simple transcription of the potential responses from the interviewer-led questionnaire into a paper version. Research participants found it as easy to complete as the other questionnaires, and it facilitated collection of health-related quality of life (HRQoL) data by post if individuals refused to attend for evaluation at follow-up visits.

A planned follow-up visit for assessment 3 months post rehabilitation was never instigated as it may have acted as an impetus for adherence to the exercise regime in all patients, thus clouding the difference between usual follow-up and telephone encouragement groups.

The DMEC asked that the effect of the telephone encouragement on walking distance be promoted to a co-primary outcome together with the site of

provision of pulmonary rehabilitation, and that the hypotheses be more clearly stated. Thus, whilst differences between the groups engendered by the site of rehabilitation might show a difference, we expected that any difference might be more marked at 18 months post rehabilitation.

At the first meeting of the DMEC they questioned the data used for power calculations and asked us to recalculate. This is addressed in detail in Sample size.

Recruitment was not as rapid as anticipated, and there were many dropouts between randomisation and the start of treatment. A short extension period for the study was granted.

At the time of the funding bid the incremental shuttle walking test (ISWT) was felt to be more appropriate than the 6-minute walking test for the primary outcome measurement, as it included an external source of pacing and was thus a better comparator for longitudinal testing. However, by the start of the study there was a new test available, the ESWT,[12,13] which allows people to walk at a set pace equivalent to 85% of their maximal oxygen uptake, which should take approximately 5 minutes. Subsequent walks are at the same pace, and it is therefore much more appropriate for testing changes engendered by pulmonary rehabilitation as there is the possibility of a greater magnitude of change. It is possible to collect data on both distance and time walked. We used percentage change in ESWT distance as our primary outcome variable for the acute phase of the study but, for completeness, additionally reported absolute ESWT distance and time.

In some areas, pulmonary rehabilitation is not widely offered to people over the age of 70. We will make data gained in this study available to researchers in this field to allow further exploratory analysis of the data, and this will be reported elsewhere.

Ethics and governance

The study was approved by relevant local research ethics committees and by the research governance

processes of the Sheffield Teaching Hospitals NHS Foundation Trust. An independent DMEC scrutinised trial design and conduct to ensure probity. Its members were Peter Calverley, Professor of Respiratory and Rehabilitation Medicine, University of Liverpool; Keith Abrams, Professor of Medical Statistics, University of Leicester; and Anthony Burton, a general practitioner in Doncaster.

Participants

People with COPD were recruited from respiratory clinics within the Sheffield Teaching Hospitals NHS Foundation Trust, community sources, physiotherapy clinics and self-referrals. All were seen by a respiratory physician to confirm the diagnosis of COPD according to the Global initiative for Chronic Obstructive Lung Disease (GOLD) criteria before being enrolled in the study, and to have their medication optimised. Informed consent was gained at the time of assessment for suitability for group pulmonary rehabilitation therapy by a study physiotherapist. This assessment, together with any quantitative measurement required by the study, was made in a hospital setting. This ensured that no bias was introduced.

The database

A bespoke database was held on a secure server which was backed up daily. Custom windows allowed study members to see only data that were relevant to them, only the study co-ordinator and database manager being allowed to see all fields or to amend data. Research participants were entered individually by entry of their hospital number and demographics were then imported from the hospital patient administration system (PAS). In the subsequent conduct of this long study, letters were always sent to the most recent address on PAS, and it was simple to check whether the hospital had been informed of the death of the participant before we made any telephone calls or appointments. Randomisation codes were held within the database, being allocated automatically once physician and physiotherapist had agreed the patient was suitable for rehabilitation. This system worked well.

The database automatically generated follow-up schedules and data collection sheets, and in turn information from these were promptly entered into the database. Numerical limiters and drop-down menus ensured consistency of data entry with numerical calculations from primary data being carried out within the database.

Study design

Inclusion and exclusion criteria

This trial was pragmatic in nature. Whilst we had to be sure that participants were appropriately diagnosed and receiving optimal care, we did not want to exclude people by imposing narrow criteria such as spirometric measurements or information requiring imaging techniques.

Inclusion criteria
- Diagnosis of COPD by respiratory physician, using GOLD guidelines.[14]
- Medical Research Council (MRC) grade 3 or worse dyspnoea despite optimal medical care.[15]
- Clinically stable at least 4 weeks before commencing rehabilitation.

Exclusion criteria
- Inability to hear or understand educational talks (despite use of interpreters and/or hearing aids where appropriate).
- Prognosis under 2 years from any disease.
- Long-term oxygen therapy or absolute requirement for oxygen therapy on exercise (defined as oxygen saturation in arterial blood falling below 80% during initial ISWT).
- Unstable and/or uncontrolled cardiac disease.
- Lack of informed consent.
- Musculoskeletal problems precluding exercise training.
- No access to home telephone.

Randomisation

People were randomised to receive pulmonary rehabilitation in either a hospital or a community setting. They were also randomised to receive subsequent standard care or follow-up by telephone. The trial statistician, SJW, generated the random allocation sequence using the RALLOC procedure in STATA 8 (StataCorp, College Station, Texas, USA)[16] using the 2×2 factorial design option, with variable block sizes and stratified by site (north or south). Each site had one possible hospital or two community options.

The database held the details of all those people who had been randomised, and their preferred site if randomised to community. Three weeks

before a course of rehabilitation, the database was checked and the most popular community site was booked. People were then contacted and invited to attend hospital for assessment, without knowing the venue for their rehabilitation. If they declined that appointment, another was offered later in the course of the trial.

In view of the nature of pulmonary rehabilitation it is not possible to blind research participants or assessors. Several stratagems were adopted in an effort to ensure that objectivity was maintained as rigorously as possible:

- Participants were unaware of their site of rehabilitation until they had completed all of their pre-rehabilitation assessment.
- The individuals carrying out the assessments were not part of the treatment teams.
- Research participants were asked not to divulge information regarding the site of rehabilitation in conversation during follow-up assessments.

The randomisation process was implemented successfully according to plan.

Having a choice of community venues inevitably meant that one was more popular than the other. This led to people who had chosen the less popular venue (and were randomised to community) having longer to wait before being called for their pulmonary rehabilitation.

The intervention

Each rehabilitation programme consisted of twice-weekly classes for 6 weeks. They comprised 1 hour for review, warm-up, exercise and cool-down and 1 hour for education, with the participants being encouraged to exercise between formal classes. They kept an exercise diary at home between sessions. There were 2/3 days between classes. A physiotherapy team supervised both arms of the randomisation, i.e. paired community and hospital sessions, to remove any staff bias between groups. Programmes were identical in each venue, with exercises following a protocol and a core syllabus for each of the educational aspects. An exercise booklet, individualised for the level of exercise the participant had achieved during the sessions, was provided at the end of the course of rehabilitation, and the research participants were encouraged at every opportunity to keep up with the booklet exercises.

Access to the sessions was designed to follow usual clinical practice, reflecting 'real life' conditions. Those attending hospital had the option of hospital transport or making their own way, but those receiving community treatment did not have transport provided. It had been planned to replicate the system utilised by an ongoing community pulmonary rehabilitation programme in Sheffield, which arranged for a voluntary transport organisation to collect the whole group and transport them to and from the venue. This proved impossible to organise on a city-wide basis at four different alternating venues. Instead we provided an introduction to the voluntary organisation at the time of recruitment, and facilitated information enquiries to the local public transport provider. The venues had been chosen to provide good public transport links and parking facilities, so this was a more pragmatic approach to the trial.

Sample size

The original primary outcome (later co-primary) was the percentage change in exercise capacity relative to baseline. Our power calculation was based on the percentage change in endurance shuttle walk distance, [(post rehabilitation − pre rehabilitation)/pre rehabilitation] × 100. From a study of 20 COPD patients the mean percentage change in distance walked relative to baseline was 188% [standard deviation (SD) 343%]. Assuming similar levels of variability, if a difference in mean percentage change of 100% between the community and hospital groups is considered to be of clinical and practical importance, then to have an 80% power of detecting this difference in means as statistically significant at the 5% (two-sided) level would require 186 research participants per group (372 in total). If 20% of participants are lost to follow-up then we needed to recruit and randomise 234 per group (468 in total). *Table 1* shows the sample sizes required to detect various differences in percentage change in distance walked relative to baseline between the hospital and community groups.

This calculation used a historical group of patients with a very high variability in improvement. Early in the course of the trial, the DMEC suggested that it would be appropriate to update power calculations based on the 58 participants who had already completed a post-rehabilitation assessment. The sample size adjustment was carried out in

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TABLE 1 *Sample sizes required to detect various differences in percentage change in distance walked relative to baseline in between the hospital and community groups*

Mean difference in change scores	n per group	Total
200%	48	96
175%	62	124
150%	84	168
125%	120	240
100%	186	372
75%	330	660
50%	740	1480
80% power and 5% two-sided significance.		

accordance with ICH (International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use) guidance: 'In long term trials there will usually be an opportunity to check the assumptions which underlay the original design and sample size calculations. This may be particularly important if the trial specifications have been made on preliminary and/or uncertain information. An interim check conducted on the blinded data may reveal that overall response variances, event rates or survival experience are not as anticipated. A revised sample size may then be calculated using suitably modified assumptions, and should be justified and documented in a protocol amendment and in the clinical study report.'[17]

Among these 58 people the mean distance walked at baseline (pre rehabilitation) was 307 m (SD 166 m) and 498 m (SD 387 m) at the post-rehabilitation assessment. This is an absolute increase of 191 m (SD 341 m) or a mean percentage change in distance walked relative to baseline of 75.7% (SD 118.8%). Thus, the updated estimate of the variability of the outcome is 120%. Assuming an SD of 120%, if a difference in mean percentage change of 60% between the community and hospital groups is considered to be of clinical and practical importance, to have an 80% power of detecting this difference in means as statistically significant at the 5% (two-sided) level would require 64 patients per group (128 in total), with valid distance walked data pre and post rehabilitation (*Figure 1*).

Extrapolating from the early part of the study we expected to recruit 240 people, and for 60% to have evaluable post-rehabilitation data; so that post rehabilitation there would be 144 research participants or 72 per group. This was discussed in depth with the funders and agreed. Using the revised standard deviation of 120% and original effect size of 100%, with 70 participants per group the study would have over 99% power to detect this
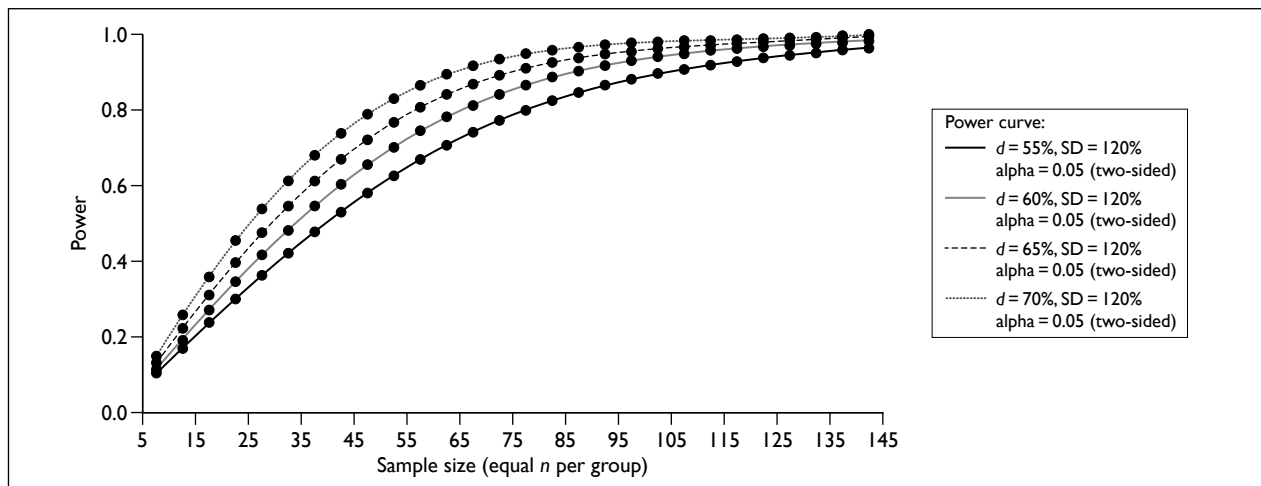

FIGURE 1 *Power size calculation. The figure shows the changing power to detect a significant difference with increasing sample size. Each curve represents a differing minimally detectable change in pre- vs post-ESWT performance, assuming a standard deviation of 120%.*

difference as statistically significant at the 5% (two-sided) level if it really existed.

Revised sample size for the SF-6D HRQoL outcome

The SF-6D health status measure is scored on a 0.30 to 1.00 'good health scale'. For the purpose of sample size estimation the main outcome will be the SF-6D preference-weighted single-index utility score post rehabilitation. This is the index that will be used in the health economic analysis.

The original sample calculation from a study in COPD patients assumed the mean SF-6D score was 0.60 (SD 0.126). Assuming similar levels of variability, if a difference in mean SF-6D scores of 0.05 between the community and hospital groups is considered to be of clinical and practical importance, to have an 80% power of detecting this difference in means as statistically significant at the 5% (two-sided) level would require 108 patients per group (216 in total), with valid SF-6D scores post rehabilitation.

However, the estimated mean SF-6D score post rehabilitation for the first 81 participants followed up in the trial is 0.63 (SD 0.11). Assuming similar

levels of variability, if a difference in mean SF-6D scores of 0.05 between the community and hospital groups is considered to be of clinical and practical importance, to have an 80% power of detecting this difference in means as statistically significant at the 5% (two-sided) level would require 78 people per group (156 in total), with valid SF-6D scores post rehabilitation. See *Table 2* for more details.

Site of rehabilitation

Our hypothesis was that a hospital venue is a place associated with ill health, where patients will go to have something done to them. Conversely a community venue is a place associated with good health, where people go to do something for themselves. The latter was therefore more likely to engender a feeling of belief in one's ability to keep exercising. We were unable to secure leisure centres where people may later join in with an ongoing class, as such a thing did not exist locally when the trial commenced. We thus rented church halls and one leisure centre. The community venues were selected to be close to public transport routes and have good parking and level access. The two hospital venues were the physiotherapy gym and a staff gym within the grounds of the hospital.

TABLE 2 *Sample sizes per group required to detect various differences in mean SF-6D scores at follow-up between the hospital and community groups using the original (0.126) and revised (0.110) standard deviations (SD) with 80% power and 5% (two-sided) significance*

| Mean difference in SF-6D score at follow-up | Original *n* per group | | Revised *n* per group randomised assuming a loss to follow-up of | | | | | |
	SD 0.126	SD 0.11	10%	20%	30%	40%	50%	60%
0.15	12	9	10	12	13	15	30	23
0.14	13	10	12	13	15	17	34	25
0.13	16	12	14	15	18	20	40	30
0.12	18	14	16	18	20	24	48	35
0.11	21	16	18	20	23	27	54	40
0.10	26	20	23	25	29	34	68	50
0.09	32	24	27	30	35	40	80	60
0.08	40	31	35	39	45	52	104	78
0.07	52	40	45	50	58	67	134	100
0.06	71	54	60	68	78	90	180	135
0.05	102	78	87	98	112	130	260	195
0.04	159	121	135	152	173	202	404	303
0.03	283	216	240	270	309	360	720	540
0.02	636	484	538	605	692	807	1614	1210
0.01	2541	1936	2152	2420	2766	3227	6454	4840

7

Pulmonary rehabilitation

The educational component was supplied by a variety of appropriate health-care professionals. It included relaxation, symptom recognition, energy conservation, the disease process and therapies. Different people provided this component in different settings, so a core programme was produced to ensure consistency.

The exercise component was delivered by physiotherapy teams, comprising a senior physiotherapist and an assistant. In order to eliminate bias, each team provided both community- and hospital-based pulmonary rehabilitation. To provide the same exercises in both settings we chose very simple regimens with easily portable equipment. This component comprised 11 workstations, with alternating upper and lower limb exercises for strength, endurance and core stability. These stations were:

- thoracic rotations (using medicine ball)
- step-ups
- shoulder punches
- knee lifts
- snow angels
- sit to stand
- bicep curls
- walking
- sweeping
- knee extensions
- lifting and pegging washing.

Exercise was individualised by both load and time. There were three different workloads for each station, patients being allocated to a workload by the result of the incremental walking test at assessment. They all started by spending 30 seconds at each workstation, recording Borg scores at the end of the exercise. They were encouraged to increase their exercise times in 15-second increments to a maximum of 2 minutes per station dependent on the Borg scores. A pulse oximeter was used at some stations to check that the oxygen saturation (SpO_2) dropped to no lower than 80%. Halfway through the 6-week programme the incremental shuttle was repeated and people were promoted to a higher workload if appropriate.

Outcomes

The primary outcome variable was the ESWT. People walk without encouragement at one of 16 predetermined speeds. The speed selected is dependent on the distance walked in the ISWT, and aims to walk people at 85% of their maximum oxygen capacity (VO_2 max), whereby they should stop after around 5 minutes' walking. This was performed at the end of the visit so that the patient was always subjected to the same degree of bronchodilatation, and the results of the exercise test did not affect the patient's judgement when completing the HRQoL questionnaires. Spirometry was measured 30 minutes after the patients had inhaled a β_2 agonist and an anticholinergic agent, given by large volume spacing device by the 10 tidal volume breathing technique. Patients were weighed, and their height measured. Skinfold thickness was measured to calculate mid-upper arm muscle area (MUAMA), which estimates lean body mass. This area is derived from the triceps skinfold thickness (TSF) and mid-upper arm circumference. Both are measured at the same site, with the patient's right arm in a relaxed position. The average mid-upper arm circumference is about 32 ± 5 cm for men and 28 ± 6 cm for women. The formula for calculating the MUAMA in cm^2 is shown below.

$$\frac{[\text{midarm circumference (cm)} - (3.14 \times \text{TSF cm})]^2}{4\pi}$$

$$- 10 \text{ (males) or} - 6.5 \text{ (females)}$$

This formula corrects the upper arm area for fat and bone. Average values for the MUAMA are 54 ± 11 cm^2 for men and 30 ± 7 cm^2 for women. A value lower than 75% of this standard (depending on age) indicates depletion of lean body mass.[18]

Instruments used for HRQoL were the interviewer-led Guyatt CRQ (amended to self-fill for all post-rehabilitation visits) together with self-fill generic tools [Short Form (36 questions) questionnaire (SF-36) version 2 and EuroQol]. Two generic tools were chosen as it was feared that the simpler but widely used EuroQol was inadequate to reflect change. After the patient had completed these questionnaires he or she was invited to complete a global health change question 'Since your last visit, do you feel the same, better or worse?' If either of the last two were selected the patient was invited to quantify an amount of change.

The use of health-care resources was collected in order to allow health economic evaluation.

All of these measurements (apart from the global health change question) were undertaken in the 2 weeks immediately before the start of pulmonary rehabilitation, and always in the same order according to the protocol. In a long study such as this there will always be personnel changes. All personnel involved in testing were trained

by the study co-ordinator (JCW) to administer the instruments, and were independent of provision of pulmonary rehabilitation. The patient was informed of the site of the pulmonary rehabilitation sessions after testing was complete.

Follow-up testing to include all the above measures was performed in the week immediately following the last pulmonary rehabilitation session. This appointment was made by the physiotherapist in discussion with the research participant during the last visit of the intervention.

Further assessments were performed at 6, 12 and 18 months post rehabilitation. A telephone call was made to arrange an appointment for the visit. If participants declined to come to the hospital for testing they were invited to complete the quality of life and resource usage questionnaires at home and were also sent a stamped addressed envelope for return of the questionnaires. Anyone who could not be contacted by telephone was written to and invited to ring for an appointment, or at least complete the quality of life questionnaires as above.

Telephone follow-up

Research participants randomised to telephone encouragement received this 1 month post pulmonary rehabilitation and at monthly intervals for 6 months. There were then telephone calls at 9, 12 and 15 months post rehabilitation. These calls were made by study personnel at assistant physiologist level and were scripted (Appendix 3). They were orientated to giving encouragement to exercise, not general health-care advice. If the participant felt worse than at the time of the last phone call, they were encouraged to restart exercising when they felt better. Those who felt the same or better than at the last telephone call were encouraged to exercise at the same level or invited to consider doing more exercise. All calls asked if the participant was doing any new exercise.

If the person could not be contacted by telephone two further attempts were made at different times of day and then the failure was recorded.

Statistical methods
Acute effects

As the trial is a parallel group, randomised controlled trial (RCT) data were reported and presented according to the revised CONsolidated Standards Of Reporting Trials (CONSORT) statement[19] and the newly published CONSORT guidelines for pragmatic trials.[20] The statistical

analyses were performed on an intention-to-treat (ITT) basis. All statistical exploratory tests were two-tailed with a p-value lower than 0.05 regarded as statistically significant. Baseline demographic (e.g. age, gender), physical measurements [e.g. weight, height, body mass index (BMI), lung function], and HRQoL data [SF-36, CRQ and EQ-5D (an index from the EuroQol)] were summarised, tabulated and assessed for comparability between the treatment groups.

Although the study was a 2×2 factorial design, the nature of the four interventions meant that COPD patients would have rehabilitation before the telephone follow-up. The four interventions were:

1. hospital rehabilitation with no telephone follow-up
2. hospital rehabilitation with telephone follow-up
3. community rehabilitation with no telephone follow-up
4. community rehabilitation with telephone follow-up.

The data were analysed in two parts. The first part used the data immediately post rehabilitation, before the telephone follow-up intervention. For this 'acute phase' we compared only post-rehabilitation outcomes between the hospital and community rehabilitation groups, as patients had not had any telephone follow-up at this stage. For longer term outcomes we utilised the full factorial nature of the design.

The primary aim of the acute phase of the statistical analysis was to compare ESWT outcomes post rehabilitation between the hospital and community rehabilitation groups. A two independent samples t test was used to compare mean change between the groups (hospital and community) in this parameter. A 95% confidence interval (CI) for the mean difference in this parameter between the community and hospital groups was also reported.

To examine the problem of non-response/attrition bias or loss to follow-up bias, we fitted a multiple linear/logistic regression model to see if the baseline characteristics of the COPD patients varied differently between the hospital and community groups according to whether or not the patient was assessed post rehabilitation. The test of non-response bias involves examining the significance of the rehabilitation group × follow-up response status interaction term. A p-value of less than 0.05 is regarded as statistically significant.

Baseline outcome = rehabilitation group follow-up response + (rehabilitation group × follow-up response) interaction

When pre- and post-treatment measures of outcome are collected then there are three possible methods of analysis:

1. post-treatment means
2. mean changes (difference between post treatment and baseline measurement)
3. post-treatment means adjusted for baseline [using analysis of covariance (ANCOVA)].

The preferred method of analysis is using post-treatment means adjusted for baseline using ANCOVA, as this is superior to the analysis of post-treatment means and mean changes.[21] We also report the results of multiple regression or ANCOVA model, with post-rehabilitation time walked on the ESWT as the outcome, baseline time walked as the covariate and treatment group as the factor. The ordinary least squares (OLS) adjusted regression coefficient estimate for the treatment group parameter along with its 95% CI is reported.

Secondary outcomes such as HRQoL (SF-36, CRQ and EQ-5D) at post rehabilitation were compared between the hospital and community rehabilitation groups using a two independent samples *t* test. The 95% CI for the mean difference in this parameter between the community and hospital groups was also reported. These secondary outcomes were also compared in an adjusted analysis using multiple regression/ ANCOVA with post-rehabilitation HRQoL as the outcome variable, and baseline HRQoL and treatment group as covariates. The OLS adjusted regression coefficient estimate for the treatment group parameter was reported from this model along with its associated *p*-value and 95% CI.

For the primary outcome post-rehabilitation ESWT distance and time walked we also used regression methods and last observation carried forward (LOCF) to impute the missing post-rehabilitation data. For missing post-rehabilitation ESWT data using the LOCF method, the baseline ESWT data were carried forward. For the regression method we used patients with valid baseline and post-rehabilitation ESWT to predict the relationship between post-rehabilitation ESWT and baseline ESWT. These regression coefficients from this model and the baseline ESWT were used to impute a post-rehabilitation ESWT outcome.

Long-term follow-up: 2 × 2 factorial design

The main aim of the analysis was to establish whether long-term outcomes (e.g. distance walked or time walked on the ESWT; HRQoL as measured by the SF-36, CRQ and EQ-5D) 6, 12 and 18 months post rehabilitation changed differently over time after hospital or community rehabilitation or telephone or no telephone follow-up utilising the 2 × 2 factorial design of the trial. $p < 0.05$ was regarded as statistically significant. All analysis was by intention to treat.

The outcome data were longitudinal and consisted of four repeated observations over time (baseline, i.e. post rehabilitation; 6 months post rehabilitation; 12 months post rehabilitation; and 18 months post rehabilitation) on each of the patients. Therefore, a marginal generalised linear model for longitudinal data, with coefficients estimated using generalised estimating equations[22] with robust standard errors and an exchangeable autocorrelation matrix in STATA,[16] was used to analyse the various outcomes and allow for the longitudinal nature of the data. Estimates for the group coefficient(s) from these regression models are reported along with their associated 95% CI.

The exchangeable correlation structure corresponds to an equal correlation model, meaning that the correlations between the outcomes at different follow-up time points are equal to each other. In this analysis the following assumptions have been made: the outcomes (ESWT and HRQoL scores) are continuous variables; there is, or potentially is, a linear relationship between outcome and time; the outcome measurements, within an individual, over time are correlated with each other so that the correlations between outcome levels at various time points are the same. The marginal model does not require a balanced data set with each patient completing all the four follow-up assessments. It uses all the available outcome data to estimate the regression coefficients for the model.

Two models for each outcome were fitted in the following order:

1. Outcome = baseline + time + rehabilitation group + follow-up group + (rehabilitation group × follow-up group) interaction
2. Outcome = baseline + time + rehabilitation group + follow-up group.

As the three post-rehabilitation follow-up visits were approximately 6 months apart, time was reclassified as 1 (6 months post rehabilitation), 2 (12 months) and 3 (18 months). The group variable was coded as 0 = community rehabilitation and 1 = hospital rehabilitation. The baseline value for the outcome was the value from the post-rehabilitation assessment and not the initial pre-rehabilitation value.

Chapter 3
Efficacy of programme

Pulmonary rehabilitation is usually provided in a hospital setting and mostly includes bicycles or treadmills for endurance training. We did not use this equipment in any of our sites. Our subsequent analyses looked for difference in efficacy between settings, but did not examine the efficacy of our specific programme per se. We therefore firstly analysed the pooled outcome results of all patients. This ensured that the programme itself was similarly effective to those using slightly different methods reported in the literature, and that it was capable of producing detectable change. There was an improvement in endurance shuttle walking time from a mean of 5.7 to 10.2 minutes. This represents a mean improvement of 4.5 minutes in endurance walking time (mean difference + 4.5, ± 5.8 SD, $p < 0.001$, 95% CI 3.6 to 5.4), and is shown in *Figure 2* and *Table 3*. The table shows pooled results for pre- and post-rehabilitation ESWT for all patients in the study.

There was also an improvement in HRQoL measures post versus pre rehabilitation. The generic summary SF-6D improved significantly by 0.02 ($p = 0.007$, 95% CI 0.01 to 0.04). The EQ-5D produced an improvement of 0.04 ($p = 0.053$, 95% CI 0.00 to 0.08). The disease-specific CRQ produced an overall improvement of 1.6 ($p < 0.001$, 95% CI 0.8 to 2.0). There were similar improvements in each component domain (*Tables 4–6*). Despite the large differences produced in exercise capacity, these differences (statistically highly significant for SF-6D and CRQ) in HRQoL are only just at the threshold of minimally important differences in population terms. These differences are discussed further in Chapter 4.
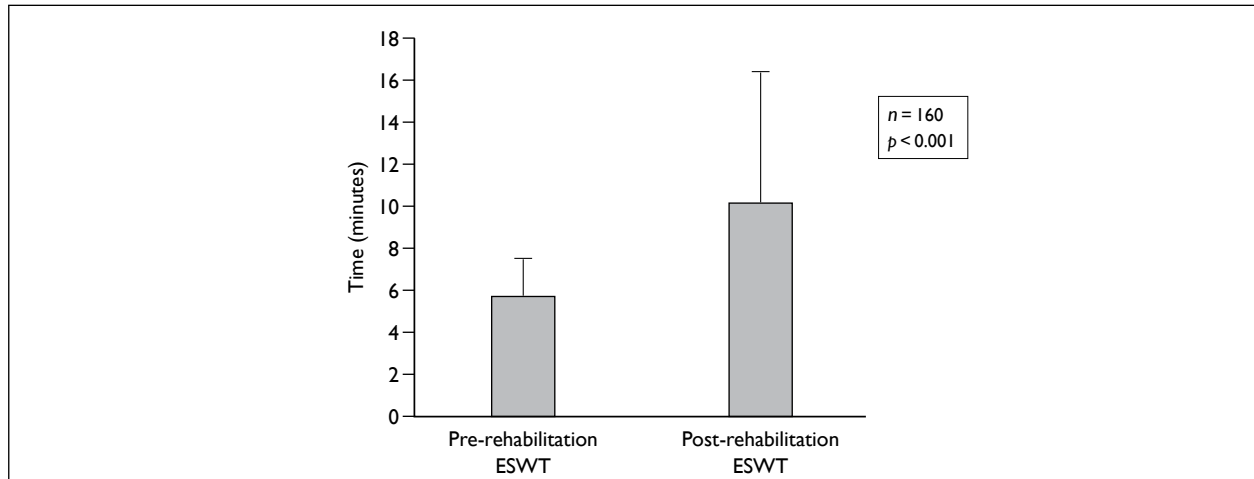
FIGURE 2 *Change in endurance shuttle walking test time pre vs post rehabilitation.*

TABLE 3 *Change in ESWT times and distanced walked after pulmonary rehabilitation – total group*

| | n | Pre rehabilitation | | Post rehabilitation | | Mean difference | 95% CI | | p-value |
		Mean	SD	Mean	SD		Lower	Upper	
Endurance distance walked (m)	161	279.7	138.3	531.2	393.2	251.6	196.9	306.2	0.001
Endurance time (minutes)	160	5.7	1.8	10.2	6.2	4.5	3.6	5.4	0.001

p-value from paired *t* test.

TABLE 4 *Change in SF-36v2 domains after pulmonary rehabilitation – total group*

	n	Pre rehabilitation		Post rehabilitation		Mean difference	95% CI		p-value
		Mean	SD	Mean	SD		Lower	Upper	
Physical functioning	171	31.9	19.2	34.4	19.9	2.5	0.0	5.0	0.049
Role–physical	171	39.8	22.9	47.8	23.8	8.0	4.1	11.8	0.001
Bodily pain	170	55.3	27.0	59.2	25.7	3.9	0.1	7.7	0.042
General health	167	34.3	18.1	37.7	20.7	3.4	0.8	5.9	0.010
Vitality	170	38.8	17.5	45.4	19.5	6.5	3.8	9.2	0.001
Social functioning	172	52.7	31.5	62.9	29.3	10.2	5.8	14.7	0.000
Role–emotional	170	59.4	30.0	66.2	30.7	6.8	1.8	11.8	0.007
Mental Health Index	171	64.0	21.4	69.9	20.0	5.9	3.4	8.4	0.001
Physical Component Summary	162	32.1	7.4	33.5	8.3	1.4	0.3	2.5	0.011
Mental Component Summary	162	43.0	12.3	47.5	12.2	4.5	2.8	6.2	0.001

p-value from paired *t* test.

TABLE 5 *Change in SF-6D and EQ-5D after pulmonary rehabilitation – total group*

	n	Pre rehabilitation		Post rehabilitation		Mean difference	95% CI		p-value
		Mean	SD	Mean	SD		Lower	Upper	
SF-6D	157	0.607	0.108	0.629	0.115	0.022	0.006	0.038	0.007
EQ-5D	171	0.590	0.258	0.628	0.257	0.038	–0.001	0.077	0.053

p-value from paired *t* test.

TABLE 6 *Change in CRQ and subdomains after pulmonary rehabilitation – total group*

	n	Pre rehabilitation		Post rehabilitation		Mean difference	95% CI		p-value
		Mean	SD	Mean	SD		Lower	Upper	
Dyspnoea	163	3.1	1.0	3.5	1.1	0.4	0.3	0.6	0.001
Fatigue	168	3.5	1.3	3.9	1.3	0.4	0.3	0.6	0.001
Emotion	166	4.4	1.4	4.7	1.3	0.3	0.1	0.5	0.001
Mastery	166	4.4	1.4	4.7	1.3	0.3	0.1	0.5	0.001
Total	157	15.6	4.0	17.2	4.0	1.6	0.8	2.0	0.001

p-value from paired *t* test.
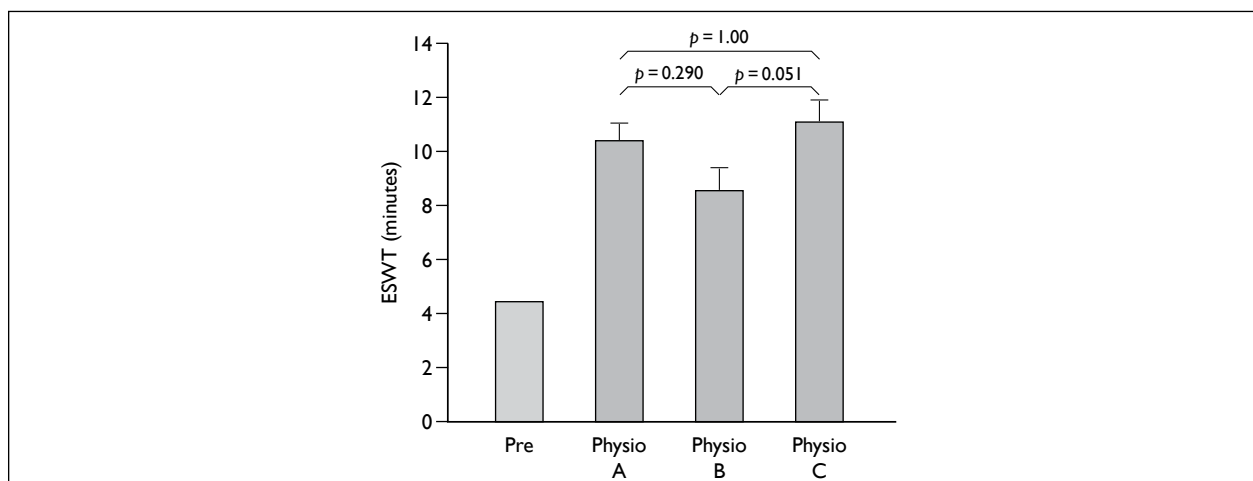
FIGURE 3 *Acute effect of pulmonary rehabilitation by treating physiotherapy team. The graph shows a post hoc analysis of post-rehabilitation endurance shuttle walking test time achieved by patients treated by physiotherapist groups A, B and C compared with pooled pre-rehabilitation times. There was no significant difference in baseline characteristics of patients treated by each team.*

Effect on acute outcome of treatment by individual physiotherapy team

During the conduct of the trial, three teams of physiotherapists delivered pulmonary rehabilitation sequentially. Each delivered care according to the trial protocol, and had been trained by the same trainers. Although each team carried out both hospital and community rehabilitation according to randomisation, we checked to ensure that there was no difference in group effect for each physiotherapy team. There was no interaction between physiotherapist and group effect, in each case being a slight trend to greater improvement in the hospital group.

Although the relative efficacy by site was similar, we were surprised to note a distinct trend to different absolute efficacy for different physiotherapy groups, which fell just short of conventional statistical significance ($p = 0.054$) after correction for pre-rehabilitation walking difference. We could detect no difference in baseline demographics to explain this. *Figure 3* shows that the difference was potentially large, e.g. the 95% CI for difference in mean endurance shuttle walking time post rehabilitation for those supervised by groups B and C was −0.007 to 5.792. This should be compared with a mean improvement of 4.2 minutes for the pooled data of all patients, i.e. the differential efficacy between pulmonary rehabilitation run by different groups could be as large as the overall mean rehabilitation effect.

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Chapter 4

Community versus hospital rehabilitation: acute effects

Results

Figure 4 shows the number of patients who were randomised and the number of patients who had valid follow-up data. Two hundred and forty patients were randomised: 111 to community and 129 to hospital rehabilitation. *Tables 7* and *8* show the baseline clinical, demographic and HRQoL characteristics of the two groups. In addition, *Table 7* shows the percentage of pulmonary rehabilitation sessions attended per group. The groups appear well matched with respect to these characteristics.

Figure 4 shows that only 68% and 66% of patients in the community and hospital rehabilitation groups respectively had follow-up data for analysis. *Tables 9–11* describe and compare the baseline clinical, demographic and HRQoL characteristics of these four groups (i.e. patients with and without follow-up data). To examine the problem of non-response/attrition bias or loss to follow-up bias we fitted a multiple linear/logistic regression model to see if the baseline characteristics of the COPD patients varied differently between the hospital and community groups according to whether or not the patient completed a post-rehabilitation assessment. The four groups appear to have broadly similar characteristics at baseline, and interaction tests found no evidence that baseline characteristics [age, ESWT, gender, BMI, forced expiratory volume in 1 second (FEV_1), HRQoL] varied significantly by treatment group or responder status.

One hundred and sixty-one research participants had valid pre- and post-rehabilitation data and were used for the analysis of the primary outcome change (pre versus post ESWT). *Table 12* shows the baseline clinical and demographic characteristics of these 161 patients, together with the percentage of pulmonary rehabilitation sessions attended. Again, the two groups (76 community and 85 hospital participants) have similar baseline characteristics.

Exploratory regression analysis failed to show any baseline demographics (age, sex) or clinical parameters (FEV_1, baseline walking distance, BMI, MUAMA) that predicted those likely to accept

rehabilitation and produce evaluable data, and allowed them to be distinguished from the group who dropped out between recruitment and first evaluation.

Primary outcome was percentage change in exercise capacity as assessed by the ESWT. Results can be expressed in two forms; the actual distance walked, or the duration. In addition to percentage change in ESWT distance, we also report absolute time and distance for ESWT for completeness to fully describe our research participants.

The primary efficacy response variable was the percentage change relative to baseline, i.e. [(end of rehabilitation − baseline)/baseline] × 100 exercise capacity.

Table 13 shows that people in the hospital rehabilitation group increased the distance they could walk at the post-rehabilitation follow-up by 283 m (SD 360 m), an increase relative to baseline of 109% (SD 137%). Patients in the community rehabilitation group increased the distance they could walk at the post-rehabilitation follow-up by 216 m (SD 340 m), an increase relative to baseline of 91% (SD 133%).

There was no statistically significant difference between the rehabilitation groups in percentage change in distance walked relative to baseline, which was 17.8% (95% CI −24.3 to 59.9, $p = 0.405$, $n = 161$).

Table 13 also shows that the hospital rehabilitation group increased the time they could walk at the post-rehabilitation follow-up by 5.0 (SD 5.9) minutes, an increase relative to baseline of 89.7% (SD 108.6%). Patients in the community rehabilitation group increased the time they could walk at the post-rehabilitation follow-up by 3.9 (SD 5.7) minutes, an increase relative to baseline of 76.2% (SD 110.2%). The observed difference between the two groups in the change in time walked relative to baseline was 13.5% (95% CI −20.8 to 47.7, $p = 0.438$, $n = 160$) in favour of

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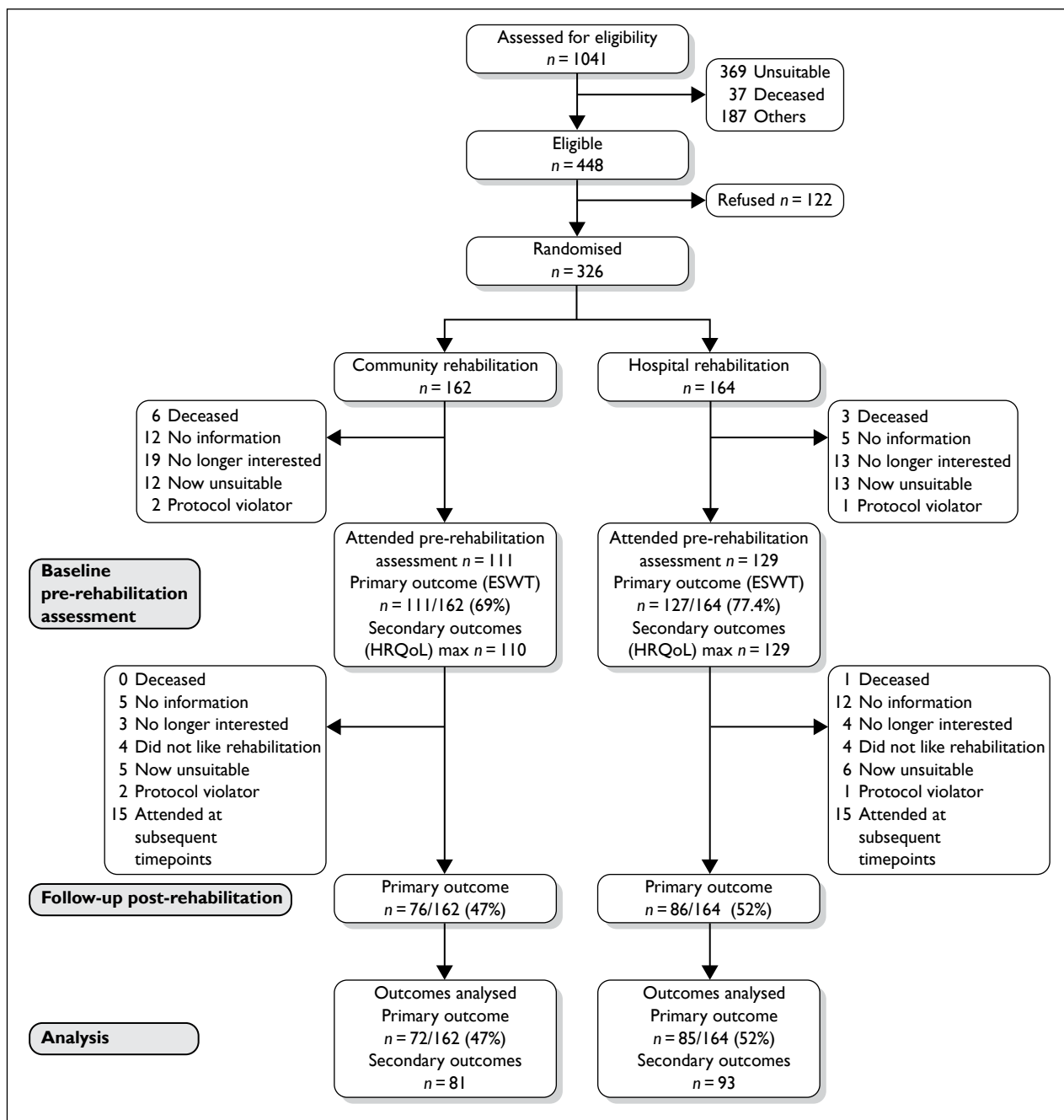
FIGURE 4 *Patient numbers available for analysis – CONSORT flow chart.*

hospital rehabilitation, although this difference was not statistically significant.

There was no statistical difference between attendance at pulmonary rehabilitation sessions between the community and hospital venues.

The preferred method of analysis is using post-treatment means adjusted for baseline using ANCOVA, as this is superior to the analysis of post-treatment means and the mean changes. *Table 14* shows the results of ANCOVA by post-

rehabilitation ESWT outcomes (distance and time walked). There was no evidence of a statistically significant difference between the rehabilitation groups on either the simple unadjusted analysis (comparison of post-rehabilitation mean distance walked) or the adjusted analysis (adjusted for baseline value of the outcome). The adjusted mean difference in distance walked was 67.8 m (95% CI –41.0 to 176.6, $p = 0.22$, $n = 161$). There was no evidence of a statistically significant difference between the rehabilitation groups on either the simple unadjusted analysis (comparison of post-

TABLE 7 Baseline demographic and clinical characteristics by rehabilitation group (all patients n = 240)

	Community rehabilitation					Hospital rehabilitation				
	n	Mean	SD	Minimum	Maximum	n	Mean	SD	Minimum	Maximum
Age (years)	111	68.7	8.3	49.0	86.0	129	69.1	7.5	51.0	85.0
Weight (kg)	111	69.4	15.9	34.4	111.0	129	69.9	20.1	35.8	143.0
Height (m)	111	1.7	0.1	1.4	1.9	129	1.7	0.1	1.5	1.9
Body mass index (kg/m^2)	111	25.4	5.6	14.0	44.0	129	25.4	5.9	15.0	42.0
FEV$_1$ (litres)	111	1.1	0.4	0.3	2.6	128	1.1	0.5	0.4	2.7
Predicted FEV$_1$ (litres)	111	2.4	0.6	1.0	3.8	129	2.4	0.6	1.1	3.8
Actual FEV$_1$ as a proportion of predicted FEV$_1$ (%)	111	45.1	16.3	16.8	89.8	128	48.3	19.3	17.4	117.8
FVC (litres)	111	2.7	0.9	1.2	5.3	128	2.7	0.9	0.9	5.0
Actual FVC as a proportion of predicted FVC (%)	111	86.7	19.3	50.8	137.5	128	90.2	19.8	42.6	155.1
Predicted FVC (litres)	111	3.1	0.8	1.3	4.8	129	3.0	0.9	1.5	5.0
Peak expiratory flow (litres/minute)	111	214.2	87.2	69.0	491.0	128	222.9	89.2	58.0	471.0
Relaxed vital capacity (litres)	111	2.7	0.9	1.4	5.1	128	2.7	0.9	1.0	5.5
FEV$_1$/FVC	111	0.4	0.1	0.2	1.0	128	0.4	0.1	0.2	0.9
Endurance distance walked (m)	111	262.8	151.3	20.0	730.0	127	270.5	138.0	20.0	700.0
Endurance time (minutes)	110	5.4	2.1	1.3	12.0	127	5.6	2.0	1.0	14.6
Arm circumference (mm)	110	283.9	48.6	152.0	455.0	125	282.7	47.2	137.0	410.0
Skinfold thickness (mm)	110	17.6	8.3	4.0	38.0	125	16.6	8.1	4.8	39.0
Mid-upper arm muscle area (cm^2)	110	34.5	14.4	5.5	88.2	125.0	35.2	13.4	7.1	74.1
Percentage of rehabilitation sessions attended	111	62.5	37.3	0.0	100.0	129	64.6	36.4	0.0	100.0
	n	%				n	%			
Gender										
Female	49	44				66	51			
Male	62	56				63	49			
Total	111	100				129	100			
MRC breathlessness grade										
3	38	34				48	38			
4	37	33				39	30			
5	36	32				41	32			
Total	111	100				128	100			

MRC, Medical Research Council.

TABLE 8 *Baseline HRQoL outcomes by rehabilitation group (n = 240)*

| | | Rehabilitation group | | | | | |
| | | Community | | | Hospital | | |
	Dimension	*n*	Mean	SD	*n*	Mean	SD
SF-36v2	Physical functioning (0–100)	108	29.8	20	128	31.0	20
	Role–physical (0–100)	110	33.1	22	128	39.9	24
	Bodily pain(0–100)	107	55.0	28	128	52.5	26
	General health (0–100)	108	33.3	18	126	32.6	18
	Vitality (0–100)	109	37.2	18	128	38.1	17
	Social functioning (0–100)	110	45.2	31	128	50.1	33
	Role–emotional (0–100)	110	53.1	30	127	57.8	31
	Mental Health Index (0–100)	110	63.0	21	128	61.7	22
	Physical Component Summary	103	31.3	7.4	126	31.9	7.3
	Mental Component Summary	103	40.7	12	126	42.0	13
	SF-6D preference-based measured of health	103	0.59	0.11	124	0.59	0.11
EQ-5D	Overall utility (tariff)	110	0.52	0.28	127	0.56	0.27
CRQ	Dyspnoea	109	3.1	0.9	127	3.0	1.0
	Fatigue	110	3.2	1.2	129	3.4	1.3
	Emotion	110	4.3	1.3	128	4.3	1.4
	Mastery	110	4.3	1.3	129	4.2	1.4
	Total	109	3.8	1.0	126	3.8	1.1

For the SF-36 and EQ-5D, a higher score indicates a better HRQoL.
The CRQ dimensions are scored on a seven point scale ranging from 1, which indicates maximum impairment, to 7, which indicates no impairment.

rehabilitation mean time walked) or the adjusted analysis (adjusted for baseline value of the outcome), the adjusted mean difference in time walked being 1.1 minutes (95% CI –0.7 to 2.9, $p = 0.25$, $n = 160$).

Table 15 shows the results of the analysis of the secondary HRQoL outcomes. There was no evidence of a statistically significant difference between the rehabilitation groups on either the simple unadjusted analysis (comparison of post-rehabilitation mean HRQoL scores) or the adjusted analysis (adjusted for baseline value of the outcome).

Figure 5 shows how we can interpret the observed study results in relation to the mean difference and 95% confidence limits, and how these appear in relation to the null (zero value) of no treatment difference and the pre-specified minimum important difference in outcomes.[23]

The CONSORT flow diagram of *Figure 4* shows that 238 COPD (111 community, 127 hospital) patients

had pre-rehabilitation (baseline) ESWT distance walked data. However at post rehabilitation, only 161/238 (67%) had valid ESWT distance walked data. Two methods of missing data imputation were used to impute the missing ESWT data for these 77 COPD patients: LOCF and regression. *Table 16* shows the results of the missing data imputation analysis and compares them with the original non-imputed data. *Figures 6* and *7* show the results graphically alongside the original data. The missing data methods tend to reduce the treatment effect and move the data towards the null value of no difference in treatments. *Figure 6* also shows the minimum clinically important difference (MID) in percentage change in distance walked relative to baseline on the ESWT between the rehabilitation groups. The ESWT does not have a clearly defined MID. Our original power calculations assumed 100% difference as being clinically important. Subsequent examination of our own data suggests that a more conservative estimate of 60% may be more appropriate (see Appendix 4). We therefore use this difference of 60% or more in percentage change in distance walked relative to baseline on

TABLE 9 Comparison of the baseline (pre-rehabilitation) clinical and demographic characteristics of the groups by post-rehabilitation follow-up status: completer or non-completer (n = 240)

| | Non-completer | | | | | | | | | Completer | | | | | | | | |
| | Community | | | Hospital | | | Group total | | | Community | | | Hospital | | | Group total | | |
	n	Mean	SD	n	Mean	SD	n	Mean	SD	n	Mean	SD	n	Mean	SD	n	Mean	SD
Age (years)	35	69.4	8.7	44	69.6	7.8	79	69.5	8.2	76	68.4	8.2	85	68.8	7.4	161	68.6	7.7
Weight (kg)	35	66.1	15.0	44	70.1	18.3	79	68.3	16.9	76	70.9	16.2	85	69.8	21.1	161	70.3	18.9
Height (m)	35	1.6	0.1	44	1.7	0.1	79	1.6	0.1	76	1.7	0.1	85	1.6	0.1	161	1.7	0.1
Body mass index (kg/m^2)	35	24.7	5.4	44	25.5	5.3	79	25.1	5.3	76	25.8	5.7	85	25.3	6.2	161	25.6	6.0
FEV$_1$ (litres)	35	1.0	0.4	44	1.1	0.5	79	1.0	0.4	76	1.1	0.4	84	1.1	0.5	160	1.1	0.5
Predicted FEV$_1$ (litres)	35	2.4	0.6	44	2.4	0.6	79	2.4	0.6	76	2.5	0.6	85	2.4	0.7	161	2.5	0.6
FVC (litres)	35	2.6	0.8	44	2.5	0.7	79	2.5	0.8	76	2.7	0.9	84	2.8	1.0	160	2.7	1.0
Predicted FVC (litres)	35	3.0	0.8	44	3.0	0.8	79	3.0	0.8	76	3.1	0.8	85	3.1	0.9	161	3.1	0.9
PEF (litres/minute)	35	195.1	70.7	44	211.6	89.7	79	204.3	81.8	76	223.0	92.9	84	228.8	88.9	160	226.0	90.6
Relaxed vital capacity (litres)	35	2.6	0.9	44	2.6	0.8	79	2.6	0.8	76	2.7	0.9	84	2.8	1.0	160	2.8	0.9
Endurance distance walked (m)	35	224.3	174.7	42	253.6	133.2	77	240.3	153.1	76	280.5	136.9	85	278.9	140.3	161	279.7	138.3
Endurance time (minutes)	35	5.1	2.8	42	5.2	2.1	77	5.2	2.4	75	5.6	1.6	85	5.8	2.0	160	5.7	1.8
Arm circumference (mm)	35	277.5	45.4	40	284.8	46.1	75	281.4	45.6	75	286.8	50.1	85	281.7	48.0	160	284.1	48.9
Skinfold thickness (mm)	35	17.3	8.0	40	16.7	7.0	75	17.0	7.4	75	17.7	8.5	85	16.6	8.6	160	17.1	8.5
Mid-upper arm muscle area (cm^2)	35	32.3	13.3	40	36.0	12.1	75	34.3	12.7	75	35.5	15.0	85	34.8	14.0	160	35.1	14.4

TABLE 10 *Comparison of the baseline (pre-rehabilitation) clinical and demographic characteristics of the groups by post-rehabilitation follow-up status: completer or non-completer (n = 240)*

	Non-completer			Completer		
	Community	Hospital	Total	Community	Hospital	Total
Gender						
Female	16	26	42	33	40	73
	45.7%	59.1%	53.2%	43.4%	47.1%	45.3%
Male	19	18	37	43	45	88
	54.3%	40.9%	46.8%	56.6%	52.9%	54.7%
Total	35	44	79	76	85	161
MRC breathlessness grade						
3	18	21	39	20	27	47
	51.4%	48.8%	50.0%	26.3%	31.8%	29.2%
4	8	7	15	29	32	61
	22.9%	16.3%	19.2%	38.2%	37.6%	37.9%
5	9	15	24	27	26	53
	25.7%	34.9%	30.8%	35.5%	30.6%	32.9%
Total	35	43	78	76	85	161

A completer is one who has a measurement made both pre and post pulmonary rehabilitation.

the ESWT between the rehabilitation groups when inspecting our results. For the observed data the upper limit of the 95% CI is just inside the 60% MID. This shows that not only is the difference not statistically significant overall (as the CI includes zero) but also there is unlikely to be a clinical important difference [see *Figure 5* condition (e)]. The two missing data imputation methods further support the view that the difference is not statistically significant and not clinically important and that the two forms of rehabilitation, hospital and community, are broadly similar or equivalent. However, if the MID changes, for example it is reduced to 40%, then the interpretation of the results clearly changes as well.

Table 15 shows there were no statistically significant differences in any measure of HRQoL between groups.

A mean difference of five or more points between the groups on the SF-36 dimensions is regarded as the MID.[24] The broad CIs in some domains (which include a five-point difference) admit the possibility that a clinical difference might be detected in a more highly powered study [condition (d) in *Figure 5*].

A mean difference of 2.0 or more points between the groups on the CRQ total or 0.5 on each of its domains is regarded as the MID.[41] This is just included within the 95% CI for two domains, which cannot exclude the possibility a clinical difference might be detected in a more highly powered study, although this is unlikely.

A mean difference of 0.04 or more points between the groups on the SF-6D utility measures is regarded as the MID.[25] This is just included within the 95% CI, which cannot exclude the possibility a clinical difference might be detected in a more highly powered study, although this is unlikely.

A mean difference of 0.07 or more points between the groups on the EQ-5D utility measures is regarded as the MID.[25] This is just included within the 95% CI, which cannot exclude the possibility a clinical difference might be detected in a more highly powered study, although this is unlikely.

Global health change

After all the HRQoL questionnaires, participants were asked post rehabilitation to rate their overall HRQoL as the same, better or worse, since before they started rehabilitation. *Table 17* and *Figure 8*

TABLE 11 Comparison of the baseline (pre-rehabilitation) HRQoL characteristics of the groups by post-rehabilitation follow-up status: completer or non-completer (n = 240)

	Non-completer									Completer								
	Community			Hospital			Group total			Community			Hospital			Group total		
	n	Mean	SD	n	Mean	SD	n	Mean	SD	n	Mean	SD	n	Mean	SD	n	Mean	SD
SF-36v2: Physical functioning (0–100)	33	24.9	17.5	44	29.1	23.3	77	27.3	21.0	75	32.0	20.3	84	32.0	18.5	159	32.0	19.3
SF-36v2: Role–physical (0–100)	34	25.2	20.4	44	34.8	24.5	78	30.6	23.2	76	36.6	22.0	84	42.6	23.5	160	39.8	22.9
SF-36v2: Bodily pain (0–100)	33	47.8	28.0	44	49.0	24.3	77	48.5	25.8	74	58.2	27.9	84	54.3	26.9	158	56.2	27.3
SF-36v2: General health (0–100)	34	28.4	17.3	43	30.8	17.9	77	29.8	17.6	74	35.6	18.7	83	33.6	18.1	157	34.5	18.3
SF-36v2: Vitality (0–100)	34	33.8	17.9	44	36.8	18.7	78	35.5	18.3	75	38.7	18.6	84	38.8	16.3	159	38.8	17.4
SF-36v2: Social functioning (0–100)	34	35.3	27.8	44	42.0	34.1	78	39.1	31.5	76	49.7	30.8	84	54.3	31.6	160	52.1	31.2
SF-36v2: Role–emotional (0–100)	34	41.9	28.4	44	53.8	33.0	78	48.6	31.4	76	58.1	29.8	83	59.9	30.5	159	59.1	30.1
SF-36v2: Mental Health Index (0–100)	34	58.4	17.7	44	59.0	22.4	78	58.7	20.4	76	65.1	21.5	84	63.1	21.2	160	64.1	21.3
SF-36v2: Physical Component Summary	32	29.5	7.3	43	31.0	6.9	75	30.4	7.0	71	32.2	7.4	83	32.4	7.6	154	32.3	7.5
SF-36v2: Mental Component Summary	32	37.4	10.9	43	39.7	12.6	75	38.7	11.9	71	42.3	12.2	83	43.2	12.4	154	42.7	12.3
SF-6D preference-based measured of health	32	0.55	0.09	43	0.57	0.11	75	0.56	0.10	71	0.61	0.11	81	0.60	0.11	152	0.61	0.11
EQ-5D overall utility (tariff)	34	0.45	0.29	43	0.47	0.27	77	0.46	0.28	76	0.56	0.27	84	0.61	0.25	160	0.59	0.26
CRQ: dyspnoea	34	3.0	0.9	43	2.9	0.8	77	2.9	0.9	75	3.2	0.9	84	3.1	1.0	159	3.2	1.0
CRQ: fatigue	35	3.0	1.1	44	3.0	1.1	79	3.0	1.1	75	3.3	1.2	85	3.6	1.3	160	3.5	1.3
CRQ: emotion	35	4.3	1.3	43	4.0	1.4	78	4.1	1.4	75	4.4	1.3	85	4.5	1.5	160	4.4	1.4
CRQ: mastery	35	4.3	1.1	44	3.9	1.4	79	4.1	1.3	75	4.3	1.4	85	4.4	1.3	160	4.4	1.3
CRQ: total	34	14.8	3.6	42	14.0	4.0	76	14.4	4.0	75	15.6	4.0	84	15.6	4.4	159	15.6	4.0

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TABLE 12 *Baseline demographic and clinical characteristics by rehabilitation group – primary analysis only (n = 161)*

	Community rehabilitation					Hospital rehabilitation				
	n	**Mean**	**SD**	**Minimum**	**Maximum**	*n*	**Mean**	**SD**	**Minimum**	**Maximum**
Age (years)	76	68.4	8.2	49.0	86.0	85	68.8	7.4	51.0	85.0
Weight (kg)	76	70.9	16.2	39.8	111.0	85	69.8	21.1	35.8	143.0
Height (m)	76	1.7	0.1	1.5	1.9	85	1.6	0.1	1.5	1.9
Body mass index (kg/m^2)	76	25.8	5.7	17.0	44.0	85	25.3	6.2	15.0	42.0
FEV$_1$ (litres)	76	1.1	0.4	0.3	2.6	84	1.1	0.5	0.4	2.7
Predicted FEV$_1$ (litres)	76	2.5	0.6	1.4	3.8	85	2.4	0.7	1.1	3.8
Actual FEV$_1$ as a proportion of predicted FEV$_1$ (%)	76	45.7	16.5	16.8	89.8	84	48.6	18.3	20.3	108.5
FVC (litres)	76	2.7	0.9	1.2	5.0	84	2.8	1.0	0.9	5.0
Actual FVC as a proportion of Predicted FVC (%)	76	85.7	18.2	50.8	132.1	84	92.1	20.1	42.6	155.1
Predicted FVC (litres)	76	3.1	0.8	1.7	4.8	85	3.1	0.9	1.5	5.0
Peak expiratory flow (litres/minute)	76	223.0	92.9	69.0	491.0	84	228.8	88.9	72.0	471.0
Relaxed vital capacity (litres)	76	2.7	0.9	1.4	5.0	84	2.8	1.0	1.3	5.5
FEV$_1$/FVC	76	0.4	0.1	0.2	0.8	84	0.4	0.1	0.2	0.9
Endurance distance walked (m)	76	280.5	136.9	40.0	660.0	85	278.9	140.3	50.0	700.0
Endurance time (minutes)	75	5.6	1.6	1.5	10.2	85	5.8	2.0	2.2	14.6
Arm circumference (mm)	75	286.8	50.1	152.0	455.0	85	281.7	48.0	175.0	410.0
Skinfold thickness (mm)	75	17.7	8.5	5.5	38.0	85	16.6	8.6	4.8	39.0
Mid-upper arm muscle area (cm^2)	75	35.5	15.0	5.3	88.2	85	34.8	14.0	7.1	74.1
Percentage of rehab sessions attended	76	80.8	24.5	0.0	100.0	85	83.3	20.7	0.0	100.0
	n	**%**				*n*	**%**			
Gender										
Female	33	43				40	47			
Male	43	57				45	53			
Total	76	100				85	100			
MRC breathlessness grade										
3	20	26				27	32			
4	29	38				32	38			
5	27	36				26	31			
Total	76	100				85	100			

TABLE 13 Acute phase primary outcome data post rehabilitation – ESWT

| | Rehabilitation group | | | | | | Mean difference | 95% CI | | p-value |
| | Community | | | Hospital | | | | Lower | Upper | |
	n	Mean	SD	n	Mean	SD				
Endurance distance walked (m)										
Baseline (pre rehabilitation)	76	280.5	136.9	85	278.9	140.3				
Post rehabilitation	76	496.6	371.1	85	562.2	411.7				
Change from pre to post rehabilitation	76	216.1	339.9	85	283.4	359.9	67.3	–42.0	176.6	0.226
Percentage change relative to baseline	76	90.95	133.4	85	108.7	136.5	17.8	–24.3	59.9	0.405
Endurance time walked (minutes)										
Baseline (pre rehabilitation)	75	5.6	1.6	85	5.8	2.0				
Post rehabilitation	75	9.5	5.9	85	10.8	6.5				
Change from pre to post rehabilitation	75	3.9	5.7	85	5.0	5.9	1.1	–0.7	2.9	0.226
Percentage change relative to baseline	75	76.2	110.2	85	89.7	108.6	13.5	–20.8	47.7	0.438

TABLE 14 Acute phase primary outcome data post rehabilitation – ESWT adjusted for baseline ESWT

| | Rehabilitation group | | | | | | Unadjusted | | | | | Adjusted[b] | | | | |
| | Community | | | Hospital | | | Mean difference[c] | 95% CI | | p-value[a] | n | Mean difference[c] | 95% CI | | p-value | n_{adj} |
	n	Mean	SD	n	Mean	SD		Lower	Upper				Lower	Upper		
Distance walked (metres)	76	496.6	371.1	86	557.7	411.4	61.1	–61.1	183.3	0.325	162	67.8	–41.0	176.6	0.22	161
Time walked (minutes)	76	9.4	5.8	86	10.7	6.4	1.3	–0.6	3.2	0.189	160	1.1	–0.7	2.9	0.25	160

n, total sample size for unadjusted analysis; n_{adj}, total sample size for adjusted analysis.
a p-value from two independent samples t test.
b Mean difference adjusted for baseline value of outcome.
c Mean difference = outcome in hospital group – outcome in community group.

TABLE 15 *Comparison of post-rehabilitation HRQoL outcomes by rehabilitation group*

	Dimension	Rehabilitation group						Unadjusted					Adjusted[b]				
		Community			Hospital				95% CI					95% CI			
		n	Mean	SD	n	Mean	SD	Mean difference[c]	Lower	Upper	p-value[a]	n	Mean difference[c]	Lower	Upper	p	n_{adj}
SF-36v2	Physical functioning	81	32.6	20.2	93	35.4	19.7	2.8	−3.2	8.8	0.36	174	2.8	−1.8	7.5	0.23	171
	Role–physical	80	44.9	23.1	92	50.1	24.1	5.2	−1.9	12.4	0.15	172	2.8	−3.8	9.5	0.40	171
	Bodily pain	81	58.7	26.7	92	59.8	25.1	1.1	−6.7	8.8	0.79	173	3.1	−3.5	9.7	0.35	170
	General health	80	38.2	21.8	92	36.4	19.5	−1.9	−8.1	4.4	0.56	172	−1.4	−6.3	3.6	0.59	167
	Vitality	81	46.5	20.2	91	44.4	18.8	−2.0	−7.9	3.9	0.50	172	−2.6	−7.6	2.4	0.31	170
	Social functioning	81	62.0	29.7	92	63.6	29.0	1.5	−7.3	10.4	0.73	173	−1.5	−9.1	6.1	0.69	172
	Role–emotional	80	63.2	31.0	92	68.3	30.2	5.1	−4.2	14.3	0.28	172	4.3	−4.2	12.8	0.32	170
	Mental Health Index	81	70.7	20.5	91	69.5	19.6	−1.2	−7.3	4.8	0.69	172	−0.3	−4.7	4.2	0.91	171
	Physical Component Summary	79	32.9	7.9	91	33.8	8.7	0.9	−1.7	3.4	0.51	170	0.8	−1.2	2.9	0.43	162
	Mental Component Summary	79	47.7	12.5	91	47.4	12.0	−0.3	−4.0	3.4	0.87	170	−1.1	−4.2	1.9	0.46	162
EQ-5D	SF-6D	78	0.63	0.12	89	0.64	0.11	0.01	−0.03	0.05	0.58	167	0.01	−0.02	0.04	0.37	157
	Overall utility	81	0.62	0.29	92	0.64	0.23	0.02	−0.06	0.09	0.67	173	−0.02	−0.09	0.05	0.57	171
CRQ	Dyspnoea	75	3.5	1.1	89	3.6	1.2	0.0	−0.3	0.4	0.78	164	0.2	−0.2	0.5	0.32	163
	Fatigue	76	4.0	1.4	93	3.9	1.2	0.0	−0.4	0.4	0.90	169	−0.2	−0.5	0.1	0.25	168
	Emotion	75	4.7	1.3	92	4.7	1.2	0.0	−0.4	0.4	0.93	167	−0.1	−0.4	0.2	0.43	166
	Mastery	76	4.7	1.3	91	4.7	1.3	0.0	−0.4	0.4	0.89	167	−0.1	−0.4	0.2	0.66	166
	Total	71	4.3	1.1	87	4.3	1.0	0.0	−0.4	0.3	0.91	158	0.0	−0.3	0.2	0.74	157

n, total sample size for unadjusted analysis; n_{adj}, total sample size for adjusted analysis.
a p-value from two independent samples t test.
b Mean difference adjusted for baseline value of outcome.
c Mean difference = outcome in hospital group – outcome in community group.
For the SF-36 and EQ-5D, a higher score indicates a better HRQoL. The CRQ dimensions are scored on a seven-point scale ranging from 1, which indicates maximum impairment, to 7, which indicates no impairment.
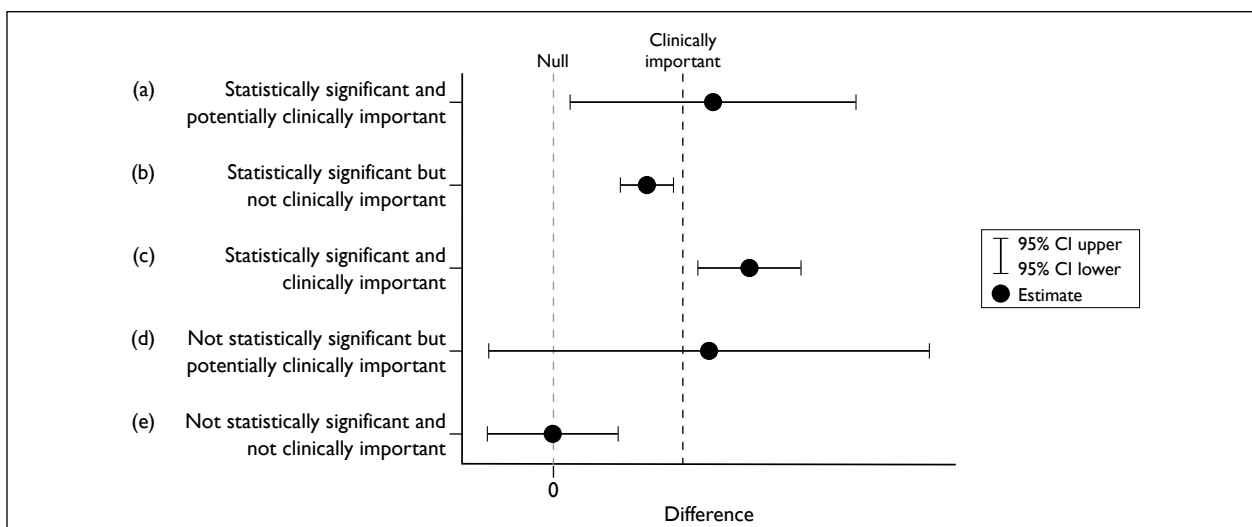
FIGURE 5 *Use of confidence intervals to help distinguish statistical significance from clinical importance.*
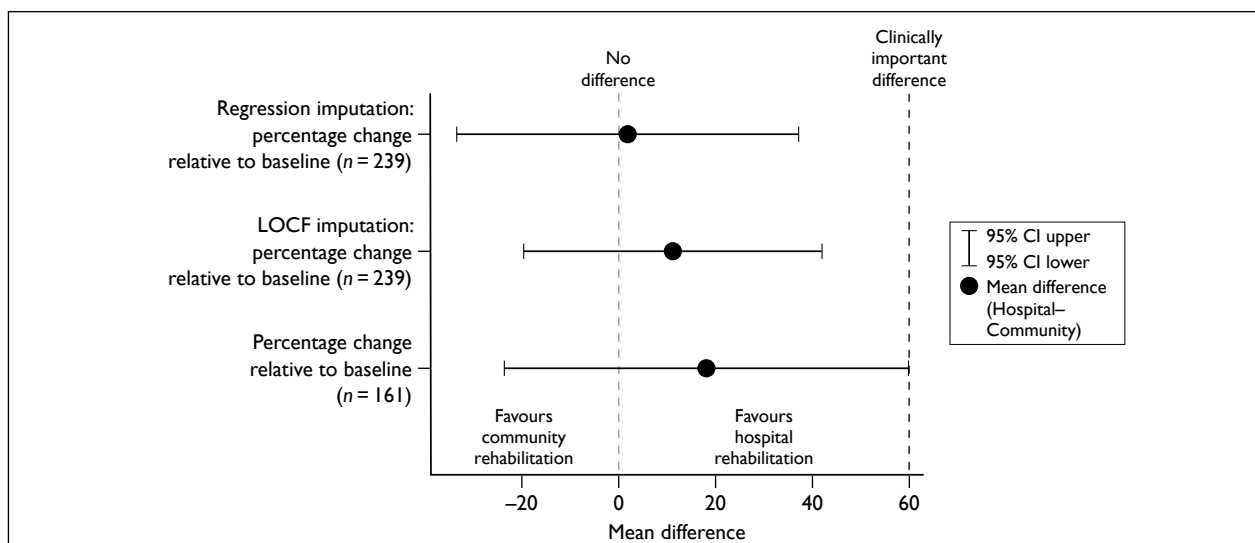
FIGURE 6 *Percentage change in endurance shuttle walking test distance walked relative to baseline with regression and LOCF imputed missing data. LOCF, last observation carried forward.*

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TABLE 16 Missing data imputation – Comparison of post-rehabilitation ESWT outcomes by rehabilitation group

		Community			Hospital			Mean difference	95% CI Lower	Upper	p-value
		n	Mean	SD	n	Mean	SD				
Endurance distance walked (m)	Baseline (pre rehabilitation)	111	262.8	151.3	127	270.5	138				
	LOCF imputed post rehabilitation	111	410.7	345.7	127	460.2	374.2				
LOCF imputation	Change from pre to post rehabilitation	111	147.9	298.3	127	189.6	322.9	41.7	−38.1	121.5	0.304
	Percentage change relative to baseline	111	62.27	118.1	127	72.78	122.8	10.5	−20.4	41.4	0.503
Endurance distance walked (m)	Baseline (pre rehabilitation)	111	262.8	151.35	127	270.5	138				
	Regression imputed post rehabilitation	111	484.5	332.62	127	540.6	352.1				
Regression imputation	Change from pre to post rehabilitation	111	221.7	282.52	127	270.1	295.4	48.4	−25.7	122.5	0.199
	Percentage change relative to baseline	111	117	143.96	127	118.4	134.9	1.5	−34.2	37.1	0.936
Endurance time walked (minutes)	Baseline (pre rehabilitation)	110	5.4	2.1	127	5.6	2				
	LOCF imputed post rehabilitation	110	8.1	5.5	127	9	6				
LOCF imputation	Change from pre to post rehabilitation	110	2.6	5	127	3.3	5.3	0.7	−0.6	2	0.306
	Percentage change relative to baseline	110	52	97.5	127	60	98.3	8.1	−17.1	33.2	0.527
Endurance time walked (minutes)	Baseline (pre rehabilitation)	110	5.4	2.1	127	5.6	2				
	LOCF imputed post rehabilitation	110	9.4	5.2	127	10.4	5.5				
Regression imputation	Change from pre to post rehabilitation	110	4	4.7	127	4.8	4.8	0.8	−0.5	2	0.218
	Percentage change relative to baseline	110	85.9	96.3	127	91.8	92.3	5.9	−18.2	30.1	0.628

LOCF, last observation carried forward imputation/regression imputation.
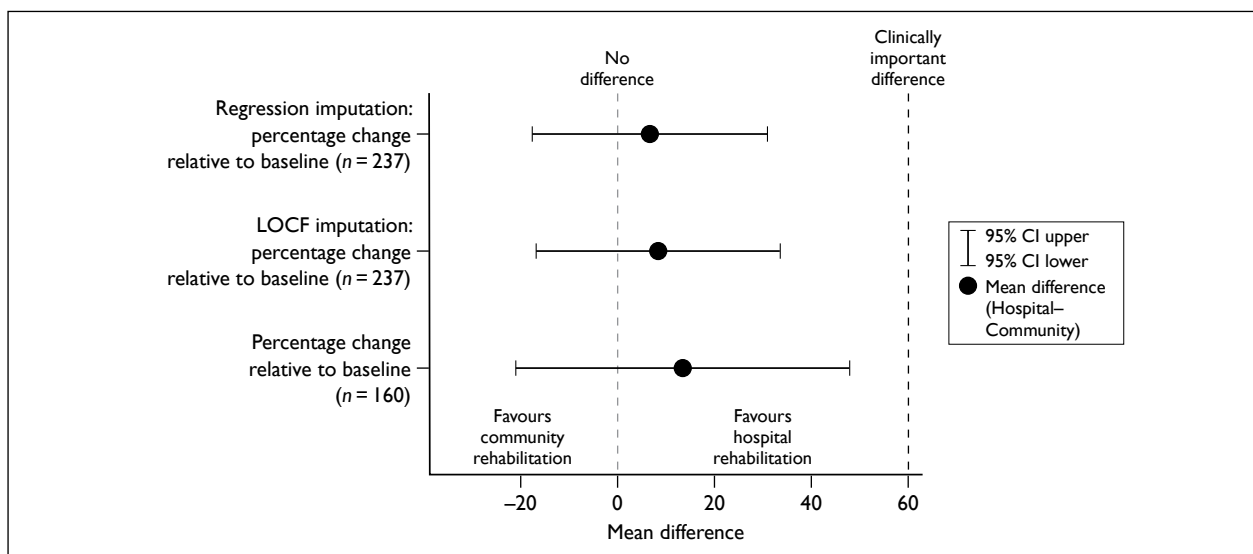
FIGURE 7 *Percentage change in endurance shuttle walking test distance time relative to baseline with regression and LOCF imputed missing data. LOCF, last observation carried forward.*

TABLE 17 *Post-rehabilitation self-reported global health change by group (n = 170)*

	Rehabilitation group					
	Community		**Hospital**		**Total**	
	n	%	*n*	%	*n*	%
Worse	8	10.3	11	12.0	19	11.2
Same	21	26.9	31	33.7	52	30.6
Better	49	62.8	50	54.3	99	58.2
Total	78	100.0	92	100.0	170	100.0

p-value from chi-squared test for trend = 0.34.
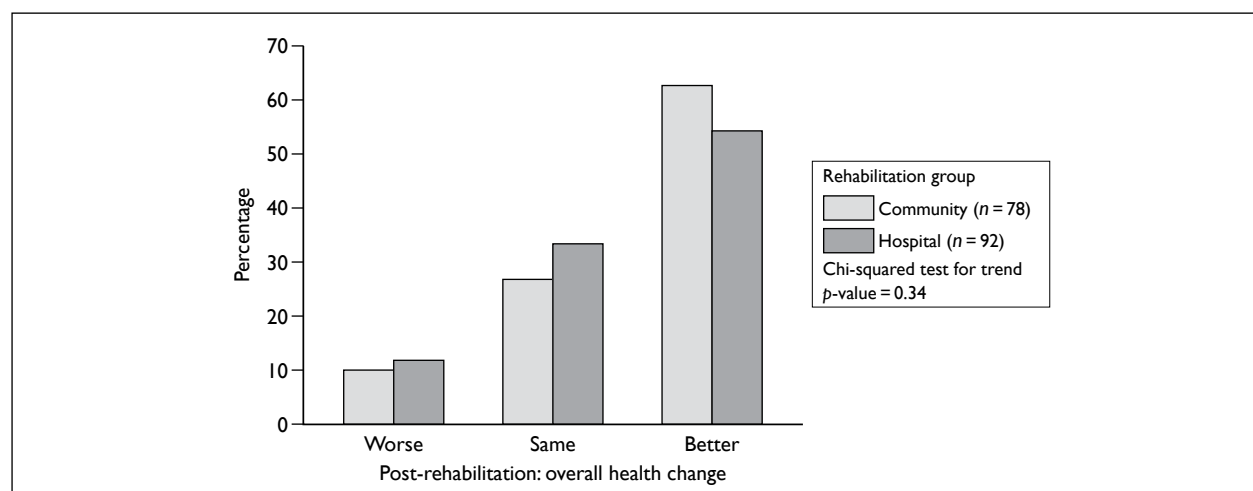
FIGURE 8 *Post-rehabilitation self-reported global health change by group (n = 170).*

show how this response varies by group. There was no statistical evidence that this outcome varied by rehabilitation group. Overall 58.2% (99/170) felt their overall HRQoL was better post rehabilitation, 88.8% (151/170) feeling that it was the same or better.

Summary of acute effects

Rehabilitation groups were well matched with respect to baseline demographic and clinical characteristics. There were no differences in treatment effects between hospital and community rehabilitation with respect to the primary efficacy response variable (the percentage change relative to baseline during the ESWT) or to secondary HRQoL outcomes. However, the CIs for some of these differences were wide. Although unlikely, potentially clinically important differences between the groups cannot be entirely excluded.

For our primary outcome measure of endurance shuttle walking distance, the minimum clinically important distance we defined a priori was outside the 95% CI. It is unlikely that this trial failed to detect a clinically important difference between the sites of pulmonary rehabilitation because of underpowering; any real difference is likely to be small.

Overall the post-rehabilitation outcomes were broadly similar between the hospital and community rehabilitation groups, although we cannot say they are exactly equivalent. The pulmonary rehabilitation programme overall, irrespective of setting, produces statistically significant improvements in outcomes post rehabilitation (endurance shuttle walk times, and HRQoL using generic and disease-specific tools).

Chapter 5
Long-term follow-up: 2 × 2 factorial design

Results

Figure 9 shows the CONSORT diagram for the follow-up of the study. As not all of the people completed the ESWT at all of the follow-up visits, this is shown separately. The diagram is complex; if someone declined to attend a follow-up visit, he or she was encouraged to complete the questionnaires at home. Declining one of the visits and/or failing to return the questionnaires did not preclude the participant from being invited to attend for subsequent follow-up visits. Some people who declined appointments attended the Respiratory Function Unit for other purposes and were also encouraged into completing as many of the follow-up tests as possible. *Tables 18* and *19* show the mean pre-rehabilitation demographic characteristics (including the percentage of possible rehabilitation sessions attended) and HRQoL scores of the four groups in the 2 × 2 factorial design. The groups were well matched. *Table 20* shows the HRQoL scores of the four groups in the 2 × 2 factorial design immediately post rehabilitation, which is now the baseline for the follow-up analysis.

Endurance shuttle walking test outcomes post rehabilitation

Figures 10 and *11* show how the ESWT distance walked varies over time (the three post-rehabilitation follow-up assessment visits). There appears to an initial increase post rehabilitation followed be a decline in distance walked over the remaining three post-rehabilitation follow-up visits.

Tables 21 and *22* shows there was no evidence of a rehabilitation group effect ($p = 0.971$). After allowing for the initial post-rehabilitation baseline distance walked, time (follow-up visit) and the factorial design (telephone follow-up group), the average difference in the post-rehabilitation follow-up distance walked on the ESWT between the hospital and community rehabilitation groups was 1.5 m (95% CI –82.1 to 97.2). Where the rehabilitation takes place (hospital or community) has no effect on the longer term (6, 12 and 18 months post rehabilitation) distance walked on the ESWT.

The longitudinal model suggests there was no evidence of a telephone follow-up group effect ($p = 0.174$). After allowing for the initial post-rehabilitation baseline distance walked, time (follow-up visit) and the factorial design (rehabilitation group), the average difference in the post-rehabilitation follow-up distance walked on the ESWT between the telephone and no-telephone groups was 56.9 m (95% CI –25.2 to 139). Telephone follow-up has no effect on the longer term (6, 12 and 18 months post rehabilitation) time walked on the ESWT in this sample of patients with COPD.

Figure 11 shows how the ESWT time walked varies over time (the three post-rehabilitation follow-up assessment visits). There appears to be an initial increase post rehabilitation followed by a decline in time walked over the remaining three post-rehabilitation follow-up visits.

Figures 12 and *13* and *Tables 23* and *24* show there was no evidence of a rehabilitation group effect ($p = 0.572$) using the ESWT time walked outcome. After allowing for the initial post-rehabilitation baseline time walked, time (follow-up visit) and the factorial design (telephone follow-up group), the average difference in the post-rehabilitation follow-up time walked on the ESWT between the hospital and community rehabilitation groups was 0.3 minutes (95% CI –0.9 to 1.6). Where the initial rehabilitation takes place (either in the hospital or out in the community) has no effect on the longer term (6, 12 and 18 months post rehabilitation) time walked on the ESWT in this sample of patients with COPD.

The longitudinal model suggests there was no evidence of a telephone follow-up group effect ($p = 0.127$). After allowing for the initial post-rehabilitation baseline time walked, time (follow-up visit) and the factorial design (rehabilitation group), the average difference in the post-rehabilitation follow-up time walked on the ESWT between the telephone and no-telephone groups was 1.0 minutes (95% CI –0.3 to 2.2). Telephone follow-up has no effect on the longer term (6, 12 and 18 months post rehabilitation) time walked on the ESWT in this sample of patients with COPD.
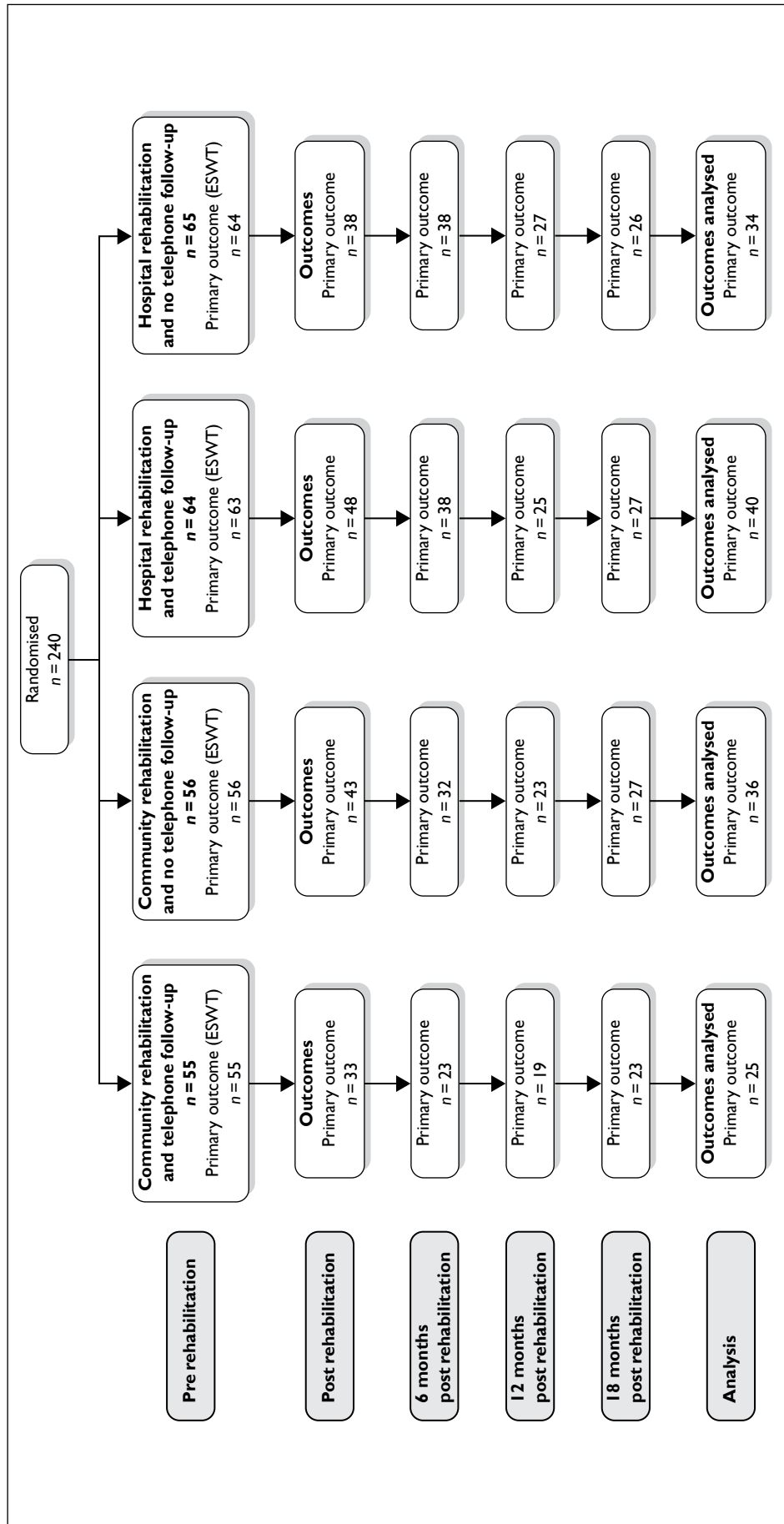
FIGURE 9 Participant numbers (with ESWT data) available for analysis – CONSORT flow chart.

TABLE 18 Pre-rehabilitation clinical and demographic characteristics of the four groups in the 2 × 2 factorial design

	Group											
	Community rehabilitation and telephone follow-up			Community rehabilitation and no telephone follow-up			Hospital rehabilitation and telephone follow-up			Hospital rehabilitation and no telephone follow-up		
	n	Mean	SD	n	Mean	SD	n	Mean	SD	n	Mean	SD
Age (years)	55	67.8	8.8	56	69.7	7.8	64	69.2	7.8	65	69	7.3
Weight (kg)	55	70.3	14.5	56	68.4	17.3	64	68.9	18.1	65	70.9	22
Height (m)	55	1.7	0.1	56	1.6	0.1	64	1.6	0.1	65	1.7	0.1
Body mass index (kg/m²)	55	25.7	5.5	56	25.2	5.8	64	25.4	6.1	65	25.4	5.8
Forced expiratory volume (FEV$_1$) in 1 second (litres)	55	1.1	0.5	56	1.1	0.4	63	1.1	0.5	65	1.2	0.5
Predicted FEV$_1$ (litres)	55	2.5	0.6	56	2.4	0.6	64	2.4	0.6	65	2.5	0.7
Forced expiratory vital capacity (FVC) (litres)	55	2.7	0.9	56	2.6	0.8	63	2.6	0.8	65	2.8	1
Predicted FVC (litres)	55	3.2	0.8	56	3	0.8	64	3	0.8	65	3.1	1
Peak expiratory flow rate (litres/minute)	55	209.2	88.4	56	219	86.5	63	212.6	80.1	65	232.9	96.7
Relaxed vital capacity (litres)	55	2.8	0.9	56	2.6	0.9	63	2.7	0.8	65	2.8	1
Endurance distance walked (m)	55	264	152.1	56	261.6	152	63	263	135.1	64	277.9	141.4
Endurance time (minutes)	54	5.5	2.2	56	5.4	2	63	5.6	2.2	64	5.7	1.9
Skinfold thickness (mm)	55	18.1	9	55	17.1	7.6	63	17.1	8.3	62	16.2	7.8
Mid-upper arm muscle area (cm²)	44	34.9	13.5	55	34.1	15.5	63	34.2	12.7	62	36.2	14.09
Percentage of rehab sessions attended	55	56.8	37.1	56	68.1	37	64	69.9	35.8	65	59.4	36.5
	n	%		n	%		n	%		n	%	
Gender												
Female	23	42		26	46		35	55		31	48	
Male	32	58		30	54		29	45		34	52	
Total	55	100		56	100		64	100		65	100	
MRC breathlessness grade												
3	23	42		15	27		24	38		24	37	
4	17	31		20	36		22	35		17	26	
5	15	27		21	38		17	27		24	37	
Total	55	100		56	100		63	100		65	100	

TABLE 19 Mean pre-rehabilitation HRQoL scores of the four groups in the 2 × 2 factorial design

	Group											
	Community rehabilitation and telephone follow-up			Community rehabilitation and no telephone follow-up			Hospital rehabilitation and telephone follow-up			Hospital rehabilitation and no telephone follow-up		
	n	Mean	SD	n	Mean	SD	n	Mean	SD	n	Mean	SD
SF-36v2: Physical functioning (0–100)	54	32.3	17.9	54	27.4	21.2	64	31.7	22.2	64	30.3	18.2
SF-36v2: Role–physical (0–100)	54	35.3	21.7	56	31.0	22.5	64	42.0	25.5	64	37.9	22.6
SF-36v2: Bodily pain (0–100)	53	55.7	27.2	54	54.3	29.4	64	54.3	24.9	64	50.6	27.2
SF-36v2: General health (0–100)	54	33.7	18.7	54	32.9	18.5	62	33.3	18.2	64	32.0	17.9
SF-36v2: Vitality (0–100)	53	38.3	18.1	56	36.0	18.9	64	36.9	17.5	64	39.4	16.7
SF-36v2: Social functioning (0–100)	54	45.8	29.8	56	44.6	31.4	64	53.9	34.1	64	46.3	31.4
SF-36v2: Role–emotional (0–100)	54	56.0	28.9	56	50.3	31.4	63	60.7	32.9	64	54.9	29.7
SF-36v2: Mental Health Index (0–100)	54	62.7	20.8	56	63.3	20.5	64	61.7	21.3	64	61.7	22.2
SF-36v2: Physical Component Summary	52	31.9	6.9	51	30.8	8	62	32.5	7.7	64	31.4	7
SF-36v2: Mental Component Summary	52	41.1	12.2	51	40.4	11.9	62	42.5	12.9	64	41.5	12.2
SF-6D preference-based measured of health	52	0.59	0.1	51	0.6	0.12	60	0.6	0.12	64	0.59	0.1
EQ-5D overall utility (tariff)	54	0.52	0.29	56	0.53	0.27	62	0.61	0.24	65	0.52	0.28
CRQ: dyspnoea	55	3.3	0.9	54	3.0	0.8	64	3.1	1.0	63	2.9	0.9
CRQ: fatigue	55	3.4	1.1	55	3.1	1.2	64	3.4	1.4	65	3.5	1.3
CRQ: emotion	55	4.4	1.4	55	4.3	1.3	64	4.4	1.5	64	4.2	1.4
CRQ: mastery	55	4.5	1.3	55	4.1	1.2	64	4.5	1.4	65	4.0	1.3
CRQ: total	55	15.8	3.9	54	14.8	3.9	64	15.5	4.4	62	14.7	4.2

For the SF-36 and EQ-5D, a higher score indicates a better HRQoL.
The CRQ dimensions are scored on a seven-point scale ranging from 1, which indicates maximum impairment, to 7, which indicates no impairment.

TABLE 20 *Mean baseline (post-rehabilitation) HRQoL scores of the four groups in the 2 × 2 factorial design*

	Group											
	Community rehabilitation and telephone follow-up			Community rehabilitation and no telephone follow-up			Hospital rehabilitation and telephone follow-up			Hospital rehabilitation and no telephone follow-up		
	n	Mean	SD	n	Mean	SD	n	Mean	SD	n	Mean	SD
SF-36v2: Physical functioning (0–100)	36	35.1	17.6	45	30.5	22.1	51	37	17.9	42	33.4	21.7
SF-36v2: Role-physical (0–100)	36	46.5	22.3	44	43.6	23.8	51	53.9	23.5	41	45.4	24.3
SF-36v2: Bodily pain (0–100)	36	58.6	25.7	45	58.8	27.7	51	63.5	25.6	41	55.1	24
SF-36v2: General health (0–100)	35	40.9	20.1	45	36.2	23	51	37.5	20.4	41	34.9	18.5
SF-36v2: Vitality (0–100)	36	48.3	18.5	45	45	21.6	51	43.9	20.7	40	45.2	16.2
SF-36v2: Social functioning (0–100)	36	64.6	23.8	45	60	33.9	51	66.9	28.5	41	59.5	29.4
SF-36v2: Role-emotional (0–100)	36	63	29.4	44	63.4	32.6	51	68	30.7	41	68.7	30
SF-36v2: Mental Health Index (0–100)	36	68.6	21.3	45	72.3	19.9	51	69.6	20.6	40	69.3	18.4
SF-36v2: Physical Component Summary	35	34.1	7.5	44	32	8.2	51	35	8.3	40	32.1	8.9
SF-36v2: Mental Component Summary	35	47.3	12.4	44	48.1	12.7	51	47.3	12.6	40	47.5	11.4
SF-6D preference-based measured of health	35	0.62	0.11	43	0.63	0.13	51	0.64	0.12	38	0.63	0.1
EQ-5D overall utility (tariff)	36	0.63	0.27	45	0.62	0.3	50	0.67	0.23	42	0.6	0.22
CRQ: dyspnoea	33	3.5	0.9	42	3.5	1.3	49	3.7	1.1	40	3.5	1.3
CRQ: fatigue	34	3.9	1.3	42	4	1.4	51	3.8	1.3	42	4.1	1.2
CRQ: emotion	34	4.6	1.3	41	4.8	1.3	51	4.6	1.3	41	4.9	1.2
CRQ: mastery	34	4.6	1.4	42	4.8	1.2	51	4.6	1.3	40	4.8	1.3
CRQ: total	32	16.5	4.3	39	17.6	4.3	49	16.8	4.2	38	17.4	4.1

For the SF-36 and EQ-5D, a higher score indicates a better HRQoL.
The CRQ dimensions are scored on a seven-point scale ranging from 1, which indicates maximum impairment, to 7, which indicates no impairment.
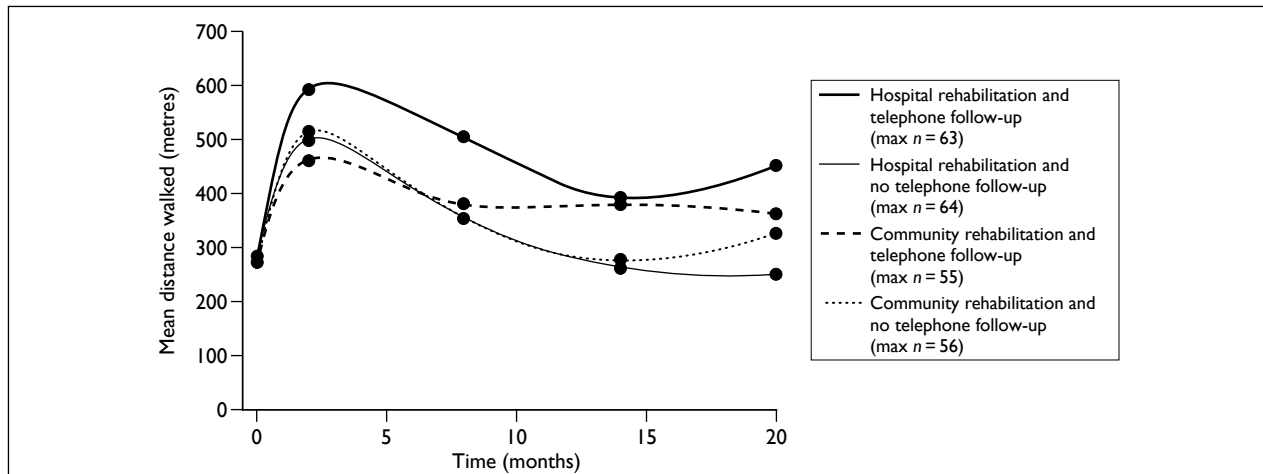
FIGURE 10 *Mean distance walked on ESWT by treatment group over time.*
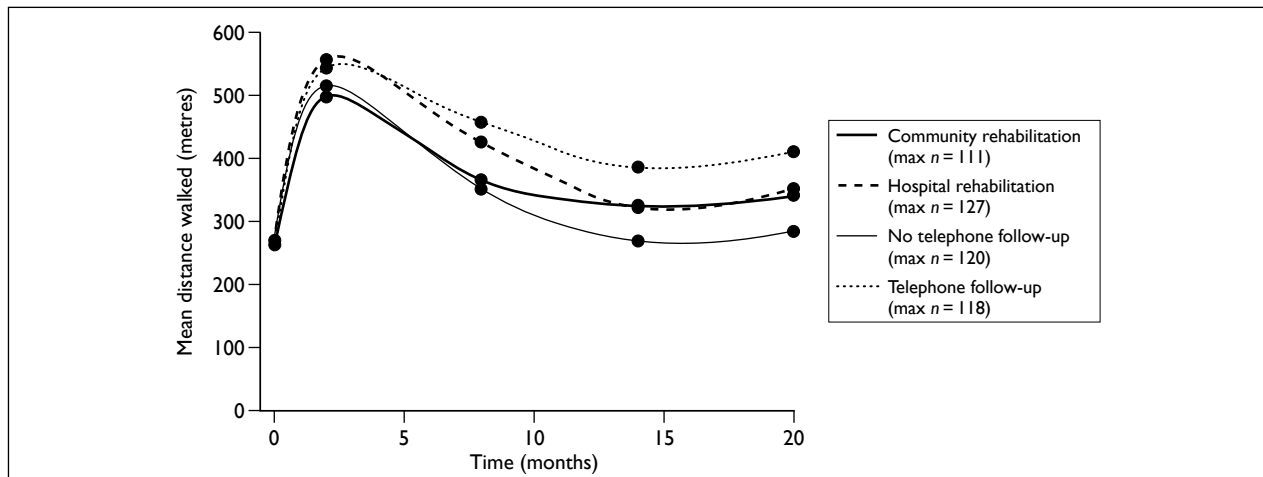
FIGURE 11 *Mean distance walked on ESWT by treatment group over time utilising the factorial design.*

Long-term quality of life outcomes post rehabilitation

Tables 25–33 show the results of analysing the HRQoL outcomes post rehabilitation. Both generic and disease-specific quality of life measures were utilised. The summary SF-6D is important as the measure that is used in health economic analyses, and the results are shown in the *Figure 14*. There was no difference between hospital and community rehabilitation groups over time after allowing for the baseline post-rehabilitation value of the outcome, time (follow-up visit) and the factorial design (adjusted group difference 0.00, 95% CI –0.02 to 0.02, $p = 0.827$). There was no significant

difference in persistent of improvement in the telephone follow-up versus usual follow-up group (adjusted group difference 0.02, 95% CI 0.00 to 0.04, $p = 0.09$). Inspection of the lower limit of the 95% CI indicates that it is exactly zero. This raises the possibility that a more highly powered study might find a statistically significant difference, although the magnitude of any likely difference is small compared with the minimum important difference.

Results for EQ-5D and the physical and mental domains of the SF-36v2 are presented in *Tables 25–28*. There were no significant differences during follow-up of these measures in either community versus hospital or telephone versus no telephone follow-up.

TABLE 21 *Results of the primary analysis distance walked (in metres) on the ESWT for the 2 × 2 factorial design with post-rehabilitation distance walked as baseline and three post-baseline follow-ups*

	Rehabilitation group						Follow-up group					
	Community			Hospital			No telephone follow-up			Telephone follow-up		
	n	Mean	SD	*n*	Mean	SD	*n*	Mean	SD	*n*	Mean	SD
Post rehabilitation (0 months)	76	496.6	371.1	86	557.7	411.4	81	512.2	379.1	81	545.8	408.1
6 months	55	366.0	332.6	76	426.8	414.8	70	350.1	340.3	61	460.0	420.6
12 months	42	323.3	305.7	52	322.5	375.5	50	267.6	276.1	44	385.7	402.3
18 months	50	341.0	365.4	53	351.3	369.3	53	286.6	284.6	50	409.6	429.4
Adjusted group difference (95% CI)[a]	−1.5 (−82.1 to 79.2)[b,d]						56.9 (−25.2 to 139.0)[c,d]					
p-value	0.971						0.174					

a Adjusted for baseline (post-rehabilitation) distance walked, time (follow-up visit) and factorial design.
b A positive difference represents a favourable outcome for the hospital group compared with the community rehabilitation group.
c A positive difference represents a favourable outcome for the telephone group compared with the no telephone follow-up group.
d The interaction between the intervention groups was investigated as a secondary analysis and was found to be non-significant [interaction coefficient = −86.0 (95% CI −249.5 to 77.4), *p* = 0.302].

TABLE 22 *Results of the primary analysis distance walked (in metres) on the ESWT for the 2 × 2 factorial design with pre-rehabilitation distance walked as baseline and four post-baseline follow-ups*

	Rehabilitation group						Follow-up group					
	Community			Hospital			No telephone follow-up			Telephone follow-up		
	n	Mean	SD	*n*	Mean	SD	*n*	Mean	SD	*n*	Mean	SD
Baseline	111	262.8	151.3	127	270.5	138	120	270.3	146.0	118	263.5	142.7
Post rehabilitation (0 months)	76	496.6	371.1	86	557.7	411.4	81	512.2	379.1	81	545.8	408.1
6 months	55	366.0	332.6	76	426.8	414.8	70	350.1	340.3	61	460.0	420.6
12 months	42	323.3	305.7	52	322.5	375.5	50	267.6	276.1	44	385.7	402.3
18 months	50	341.0	365.4	53	351.3	369.3	53	286.6	284.6	50	409.6	429.4
Adjusted group difference (95% CI)[a]	52.3 (−31.7 to 136.3)[b,d]						65.1 (−19.4 to 149.6)[c,d]					
p-value	0.222						0.131					

a Adjusted for baseline time distance walked, time (follow-up visit) and factorial design.
b A positive difference represents a favourable outcome for the hospital group compared with the community rehabilitation group.
c A positive difference represents a favourable outcome for the telephone group compared with the no telephone follow-up group.
d The interaction between the intervention groups was investigated as a secondary analysis and was found to be non-significant [interaction coefficient = 157.6 (95% CI −8.7 to 323.9), *p* = 0.063].

Disease-specific CRQ likewise failed to show any significant difference between community and hospital groups over time (adjusted difference 0.02, 95% CI −0.91 to 0.94, *p* = 0.974) (see *Tables 29–33*). *Table 29* demonstrates a significant difference in total CRQ in favour of telephone versus no telephone follow-up (adjusted difference 0.92, 95% CI 0.01 to 1.83, *p* = 0.047), although the mean difference is less than the minimum important difference. Examination of the four
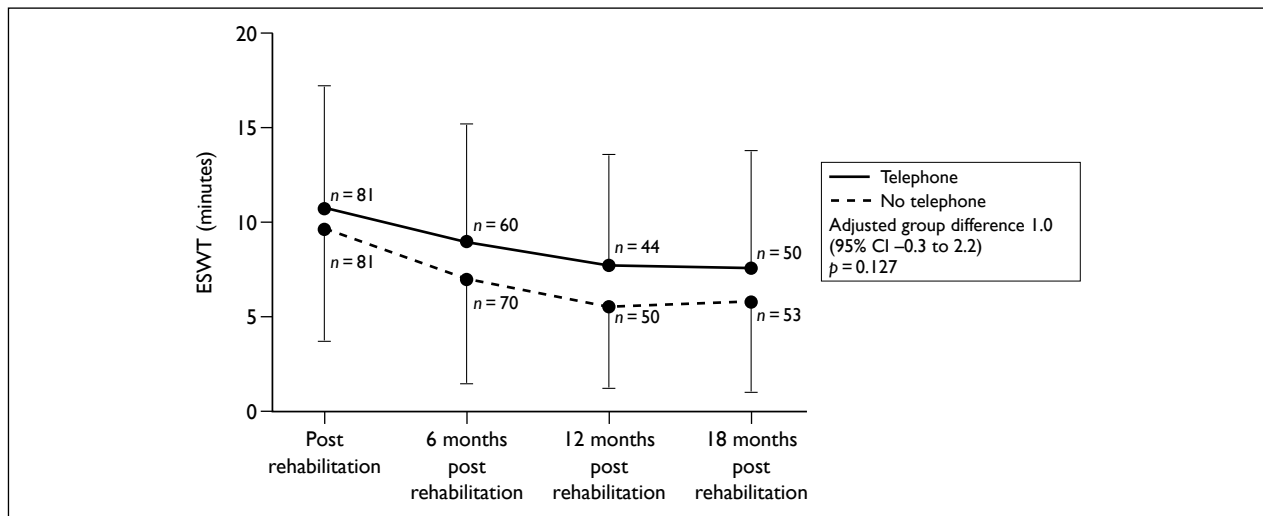
FIGURE 12 *Endurance shuttle walk time at follow-up. The graphs show the endurance shuttle walking time in telephone vs no telephone groups during 18 months of follow-up. The statistics presented refer to corrected intergroup differences as explained in the text. (Data show mean and standard deviation.)*
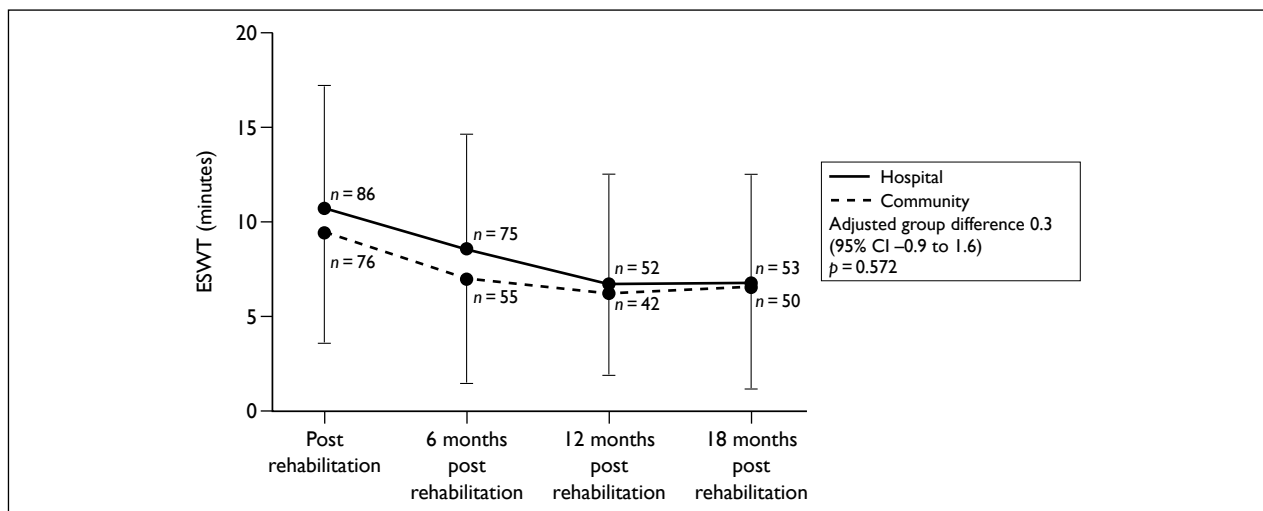
FIGURE 13 *Endurance shuttle walk time at follow-up. The graphs show the endurance shuttle walking time in hospital- vs community-treated groups during 18 months of follow-up. The statistics presented refer to corrected intergroup differences as explained in the text. (Data show mean and standard deviation.)*

domains of the CRQ shows that this difference was driven largely by a highly significant difference in mastery (adjusted difference 0.4, 95% CI 0.1 to 0.6, $p = 0.002$) (see *Table 31*). The minimum important difference for a domain of the CRQ is 0.5. The mean change in mastery is of this order. There was no significant difference in the emotional domain (adjusted difference 0.2, 95% CI 0.0 to 0.5, $p = 0.076$), The lower 95% CI is exactly zero, admitting the possibility that a more highly powered study may have found a statistically significant though small difference. Fatigue and dyspnoea domains failed to show differences.

Telephone follow-up

Eighty-one patients had one or more telephone contacts, and 80 patients had at least one valid telephone contact where they responded to the initial health status question (see Appendix 3 for details of the telephone call proforma) on 'How is your chest today, compared to how it usually is?'.

For these 80 patients the number of valid telephone contacts ranged between one and eight with a mean (and median) of five. *Figure 15* shows

TABLE 23 *Results of the primary outcome (time walked in minutes on the ESWT) for the 2 × 2 factorial trial*

	Rehabilitation group						Follow-up group					
	Community			Hospital			No telephone follow-up			Telephone follow-up		
	n	Mean	SD	*n*	Mean	SD	*n*	Mean	SD	*n*	Mean	SD
Post rehabilitation (0 months)	76	9.4	5.8	86	10.7	6.4	81	9.6	5.9	81	10.7	6.5
6 months	55	7.0	5.5	75	8.5	6.1	70	6.9	5.4	60	9.0	6.2
12 months	42	6.3	4.4	52	6.7	5.8	50	5.5	4.3	44	7.7	5.9
18 months	50	6.6	5.4	53	6.8	5.7	53	5.8	4.8	50	7.6	6.2
Adjusted group difference (95% CI)[a]	0.3 (–0.9 to 1.6)[b,d]						1.0 (–0.3 to 2.2)[c,d]					
p-value	0.572						0.127					

a Adjusted for baseline (post rehabilitation) time walked, time (follow-up visit) and factorial design.
b A positive difference represents a favourable outcome for the hospital group compared with the community rehabilitation group.
c A positive difference represents a favourable outcome for the telephone group compared with the no telephone follow-up group.
d The interaction between the intervention groups was investigated as a secondary analysis and was found to be non-significant [interaction coefficient = –0.7 (95% CI –3.2 to 1.7), *p* = 0.554].

TABLE 24 *Results of the primary outcome (time walked on the ESWT) for the 2 × 2 factorial trial*

	Rehabilitation group						Follow-up group					
	Community			Hospital			No telephone follow-up			Telephone follow-up		
	n	Mean	SD	*n*	Mean	SD	*n*	Mean	SD	*n*	Mean	SD
Baseline	110	5.429	2.075	127	5.608	2.025	120	5.529	1.912	117	5.5	2.183
Post rehabilitation (0 months)	76	9.448	5.85	86	10.73	6.437	81	9.597	5.88	81	10.7	6.465
6 months	55	7.034	5.454	75	8.469	6.128	70	6.879	5.391	60	9.0	6.242
12 months	42	6.342	4.399	52	6.693	5.767	50	5.486	4.274	44	7.7	5.865
18 months	50	6.578	5.44	53	6.827	5.692	53	5.846	4.795	50	7.6	6.161
Adjusted group difference (95% CI)[a]	1.1 (–0.3 to 2.5)[b,d]						1.4 (–0.02 to 2.8)[c,d]					
p-value	0.13						0.054					

a Adjusted for baseline time walked, time (follow-up visit) and factorial design.
b A positive difference represents a favourable outcome for the hospital group compared with the community rehabilitation group.
c A positive difference represents a favourable outcome for the telephone group compared with the no telephone follow-up group.
d The interaction between the intervention groups was investigated as a secondary analysis and was found to be significant [interaction coefficient = 3.0 (95% CI 0.2 to 5.7), *p* = 0.037].

TABLE 25 *SF-6D score for the 2 × 2 factorial design*

	Rehabilitation group						Follow-up group					
	Community			Hospital			No telephone follow-up			Telephone follow-up		
	n	Mean	SD	*n*	Mean	SD	*n*	Mean	SD	*n*	Mean	SD
Post rehabilitation (0 months)	78	0.63	0.12	89	0.64	0.11	81	0.63	0.11	86	0.63	0.12
6 months	68	0.58	0.11	88	0.61	0.11	80	0.59	0.11	76	0.60	0.12
12 months	70	0.60	0.12	78	0.59	0.10	78	0.58	0.11	70	0.62	0.12
18 months	65	0.58	0.11	88	0.58	0.10	78	0.57	0.11	75	0.59	0.09
Adjusted group difference (95% CI)[a]	0.00 (–0.02 to 0.02)[b,d]						0.02 (–0.00 to 0.04)[c,d]					
p-value	0.827						0.09					

a Adjusted for baseline SF-6D score, time (follow-up visit) and factorial design.
b A positive difference represents a favourable outcome for the hospital group compared with the community rehabilitation group.
c A positive difference represents a favourable outcome for the telephone group compared with the no telephone follow-up group.
d The interaction between the intervention groups was investigated as a secondary analysis and was found to be significant [interaction coefficient = –0.05 (95% CI –0.09 to –0.01), *p* = 0.021].
The SF-6D is scored on a 0.30–1.00 (good health) scale.

TABLE 26 *EQ-5D score for the 2 × 2 factorial design*

	Rehabilitation group						Follow-up group					
	Community			Hospital			No telephone follow-up			Telephone follow-up		
	n	Mean	SD	*n*	Mean	SD	*n*	Mean	SD	*n*	Mean	SD
Post rehabilitation (0 months)	81	0.62	0.29	92	0.64	0.23	87	0.61	0.26	86	0.65	0.25
6 months	75	0.53	0.27	94	0.59	0.24	85	0.54	0.25	84	0.59	0.26
12 months	72	0.53	0.29	96	0.55	0.24	88	0.48	0.28	80	0.60	0.23
18 months	74	0.50	0.31	95	0.54	0.26	84	0.51	0.28	85	0.53	0.27
Adjusted group difference (95% CI)[a]	0.03 (–0.02 to 0.08)[b,d]						0.02 (–0.03 to 0.07)[c,d]					
p-value	0.181						0.359					

a Adjusted for baseline EQ-5D score, time (follow-up visit) and factorial design.
b A positive difference represents a favourable outcome for the hospital group compared with the community rehabilitation group.
c A positive difference represents a favourable outcome for the telephone group compared with the no telephone follow-up group.
d The interaction between the intervention groups was investigated as a secondary analysis and was found to be non-significant [interaction coefficient = –0.06 (95% CI –0.16 to 0.04), *p* = 0.222].
The EQ-5D is scored on a –0.60 to 1.00 (good health) scale.

TABLE 27 *SF-36 Mental Component Summary (MCS) score for the 2 × 2 factorial design*

	Rehabilitation group						Follow-up group					
	Community			Hospital			No telephone follow-up			Telephone follow-up		
	n	Mean	SD	*n*	Mean	SD	*n*	Mean	SD	*n*	Mean	SD
Post rehabilitation (0 months)	79	47.7	12.5	91	47.4	12.0	84	47.8	12.0	86	47.3	12.4
6 months	69	41.2	12.6	87	45.04	12.9	78	43.4	12.7	78	43.2	13.1
12 months	69	44.1	14.2	85	42.02	12.3	81	41.6	12.8	73	44.4	13.6
18 months	67	41.5	12.9	90	40.95	12.6	78	40.7	12.2	79	41.7	13.3
Adjusted group difference (95% CI)[a]	0.8 (–1.8 to 3.4)[b,d]						0.4 (–2.1 to 2.9)[c,d]					
p-value	0.544						0.76					

a Adjusted for baseline MCS score, time (follow-up visit) and factorial design.
b A positive difference represents a favourable outcome for the hospital group compared with the community rehabilitation group.
c A positive difference represents a favourable outcome for the telephone group compared with the no telephone follow-up group.
d The interaction between the intervention groups was investigated as a secondary analysis and was found to be non-significant [interaction coefficient = –4.1 (95% CI –9.2 to 1.0), *p* = 0.119].
The MCS score is standardised to have a mean score of 50 and a standard deviation of 10 (the same as the reference population – US 1998).

TABLE 28 *SF-36 Physical Component Summary (PCS) score for the 2 × 2 factorial design*

	Rehabilitation group						Follow-up group					
	Community			Hospital			No telephone follow-up			Telephone follow-up		
	n	Mean	SD	*n*	Mean	SD	*n*	Mean	SD	*n*	Mean	SD
Post rehabilitation (0 months)	79	32.9	7.9	91	33.8	8.7	84	32.0	8.5	86	34.6	8.0
6 months	69	31.6	7.4	87	31.1	7.7	78	30.1	6.8	78	32.5	8.1
12 months	69	30.8	7.7	85	31.2	7.0	81	29.7	7.3	73	32.3	7.1
18 months	67	30.8	8.7	90	30.8	7.5	78	30.1	7.9	79	31.4	8.2
Adjusted group difference (95% CI)[a]	–0.5 (–2.0 to 1.1)[b,d]						0.7 (–0.9 to 2.3)[c,d]					
p-value	0.558						0.395					

a Adjusted for baseline PCS score, time (follow-up visit) and factorial design.
b A positive difference represents a favourable outcome for the hospital group compared with the community rehabilitation group.
c A positive difference represents a favourable outcome for the telephone group compared with the no telephone follow-up group.
d The interaction between the intervention groups was investigated as a secondary analysis and was found to be non-significant [interaction coefficient = –0.6 (95% CI –3.8 to 2.5), *p* = 0.689].
The PCS score is standardised to have a mean score of 50 and a standard deviation of 10 (the same as the reference population – US 1998).

TABLE 29 *Chronic Respiratory Questionnaire (CRQ) total score for the 2 × 2 factorial design*

| | Rehabilitation group | | | | | | Follow-up group | | | | | |
| | Community | | | Hospital | | | No telephone follow-up | | | Telephone follow-up | | |
	n	Mean	SD	*n*	Mean	SD	*n*	Mean	SD	*n*	Mean	SD
Post rehabilitation (0 months)	71	17.1	4.3	87	17.1	4.1	77	17.5	4.2	81	16.7	4.2
6 months	70	14.8	4.4	87	15.3	4.2	81	14.8	3.9	76	15.4	4.6
12 months	63	14.9	4.4	86	14.7	4.2	75	14.1	4.3	74	15.4	4.1
18 months	66	14.7	4.7	84	14.6	4.3	75	14.2	4.5	75	15.0	4.4
Adjusted group difference (95% CI)[a]	0.02 (–0.91 to 0.94)[b,d]						0.92 (0.01 to 1.83)[c,d]					
p-value	0.974						0.047					

a Adjusted for baseline CRQ total score, time (follow-up visit) and factorial design.
b A negative difference represents a favourable outcome for the hospital group compared with the community rehabilitation group.
c A negative difference represents a favourable outcome for the telephone group compared with the no telephone follow-up group.
d The interaction between the intervention groups was investigated as a secondary analysis and was found to be non-significant [interaction coefficient = 0.2 (95% CI –2.1 to 1.6), *p* = 0.822].
The CRQ total score ranges from 4, which indicates maximum impairment, to 28, which indicates no impairment.

TABLE 30 *Chronic Respiratory Questionnaire (CRQ) dyspnoea score for the 2 × 2 factorial design*

| | Rehabilitation group | | | | | | Follow-up group | | | | | |
| | Community | | | Hospital | | | No telephone follow-up | | | Telephone follow-up | | |
	n	Mean	SD	*n*	Mean	SD	*n*	Mean	SD	*n*	Mean	SD
Post rehabilitation (0 months)	75	4.7	1.3	92	4.7	1.2	82	3.5	1.3	82	3.6	1.0
6 months	74	4.3	1.4	93	4.3	1.3	83	3.0	1.0	78	3.3	1.1
12 months	70	4.3	1.4	93	4.2	1.2	79	2.9	1.2	76	3.2	1.0
18 months	73	4.1	1.4	92	4.0	1.3	77	2.9	1.1	78	3.1	1.1
Adjusted group difference (95% CI)[a]	0.0 (–0.2 to 0.3)[b,d]						0.2 (–0.1 to 0.4)[c,d]					
p-value	0.965						0.19					

a Adjusted for baseline (post-rehabilitation) CRQ dyspnoea score, time (follow-up visit) and factorial design.
b A negative difference represents a favourable outcome for the hospital group compared with the community rehabilitation group.
c A negative difference represents a favourable outcome for the telephone group compared with the no telephone follow-up group.
d The interaction between the intervention groups was investigated as a secondary analysis and was found to be non-significant [interaction coefficient = 0.1 (95% CI –0.4 to 0.6), *p* = 0.631].
The CRQ dimensions are scored on a seven-point scale ranging from 1, which indicates maximum impairment, to 7, which indicates no impairment.

TABLE 31 *Chronic Respiratory Questionnaire (CRQ) emotion score for the 2 × 2 factorial design*

| | Rehabilitation group | | | | | | Follow-up group | | | | | |
| | Community | | | Hospital | | | No telephone follow-up | | | Telephone follow-up | | |
	n	Mean	SD	*n*	Mean	SD	*n*	Mean	SD	*n*	Mean	SD
Post rehabilitation (0 months)	75	4.7	1.3	92	4.7	1.2	82	4.8	1.2	85	4.6	1.3
6 months	74	4.3	1.4	93	4.3	1.3	84	4.3	1.2	83	4.3	1.4
12 months	70	4.3	1.4	93	4.2	1.2	83	4.0	1.2	80	4.4	1.4
18 months	73	4.1	1.4	92	4.0	1.3	83	3.9	1.3	82	4.2	1.3
Adjusted group difference (95% CI)[a]	0.0 (–0.2 to 0.3)[b,d]						0.2 (–0.0 to 0.5)[c,d]					
p-value	0.749						0.076					

a Adjusted for baseline (post rehabilitation) CRQ emotion score, time (follow-up visit) and factorial design.
b A negative difference represents a favourable outcome for the hospital group compared with the community rehabilitation group.
c A negative difference represents a favourable outcome for the telephone group compared with the no telephone follow-up group.
d The interaction between the intervention groups was investigated as a secondary analysis and was found to be non-significant [interaction coefficient = –0.1 (95% CI –0.6 to 0.4), $p = 0.757$].
The CRQ dimensions are scored on a seven-point scale ranging from 1, which indicates maximum impairment, to 7, which indicates no impairment.

TABLE 32 *Chronic Respiratory Questionnaire (CRQ) fatigue score for the 2 × 2 factorial design*

| | Rehabilitation group | | | | | | Follow-up group | | | | | |
| | Community | | | Hospital | | | No telephone follow-up | | | Telephone follow-up | | |
	n	Mean	SD	*n*	Mean	SD	*n*	Mean	SD	*n*	Mean	SD
Post rehabilitation (0 months)	76	4.0	1.4	93	3.9	1.2	84	4.0	1.3	85	3.9	1.3
6 months	78	3.5	1.2	94	3.6	1.3	86	3.5	1.2	86	3.6	1.3
12 months	71	3.3	1.4	95	3.3	1.2	86	3.2	1.2	80	3.5	1.3
18 months	73	3.3	1.4	93	3.3	1.2	83	3.3	1.3	83	3.3	1.3
Adjusted group difference (95% CI)[a]	0.0 (–0.2 to 0.3)[b,d]						0.2 (–0.1 to 0.4)[c,d]					
p-value	0.790						0.145					

a Adjusted for baseline (post-rehabilitation) CRQ fatigue score, time (follow-up visit) and factorial design.
b A negative difference represents a favourable outcome for the hospital group compared with the community rehabilitation group.
c A negative difference represents a favourable outcome for the telephone group compared with the no telephone follow-up group.
d The interaction between the intervention groups was investigated as a secondary analysis and was found to be non-significant [interaction coefficient = –0.2 (95% CI –0.7 to 0.3), $p = 0.383$].
The CRQ dimensions are scored on a seven-point scale ranging from 1, which indicates maximum impairment, to 7, which indicates no impairment.

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TABLE 33 *Chronic Respiratory Questionnaire (CRQ) mastery score for the 2 × 2 factorial design*

	Rehabilitation group						Follow-up group					
	Community			Hospital			No telephone follow-up			Telephone follow-up		
	n	Mean	SD	*n*	Mean	SD	*n*	Mean	SD	*n*	Mean	SD
Post rehabilitation (0 months)	76	4.7	1.3	91	4.7	1.3	82	4.8	1.2	85	4.626	1.3
6 months	75	4.2	1.3	95	4.3	1.3	85	4.1	1.2	85	4.421	1.4
12 months	71	4.3	1.3	93	4.1	1.3	83	4.0	1.4	81	4.414	1.2
18 months	73	4.2	1.5	92	4.1	1.3	83	4.0	1.4	82	4.314	1.4
Adjusted group difference (95% CI)[1]	0.0 (–0.2 to 0.3)[b,d]						0.4 (0.1 to 0.6)[c,d]					
p-value	0.903						0.002					

a Adjusted for baseline (post-rehabilitation) CRQ mastery score, time (follow-up visit) and factorial design.
b A negative difference represents a favourable outcome for the hospital group compared with the community rehabilitation group.
c A negative difference represents a favourable outcome for the telephone group compared with the no telephone follow-up group.
d The interaction between the intervention groups was investigated as a secondary analysis and was found to be non-significant (interaction coefficient = –0.2 (95% CI –0.7 to 0.3), *p* = 0.422].
The CRQ dimensions are scored on a seven-point scale ranging from 1, which indicates maximum impairment, to 7, which indicates no impairment.

the distribution of the number of valid patient telephone contacts.

As the number of telephone contacts varied from one to eight, for each patient we calculated a series of summary measures to describe the telephone contact. For example, for each individual patient we calculated the percentage of the valid telephone calls in which the patient reported that he or she was still doing the booklet exercises. If patients reported they were still doing the exercises at each telephone contact, then this summary value would be 100%.

Table 34 reports the descriptive statistics for these summary measures of the telephone contact data. For example, patients reported that on average for 61% of telephone contacts they were still doing the booklet exercises and for 69% of telephone contacts they reported they were still doing other exercises as well. At 10% of their telephone contacts, patients reported increasing their exercise times.

For 65% of the telephone contacts, patients reported their chest today as being the same or better (than usual).
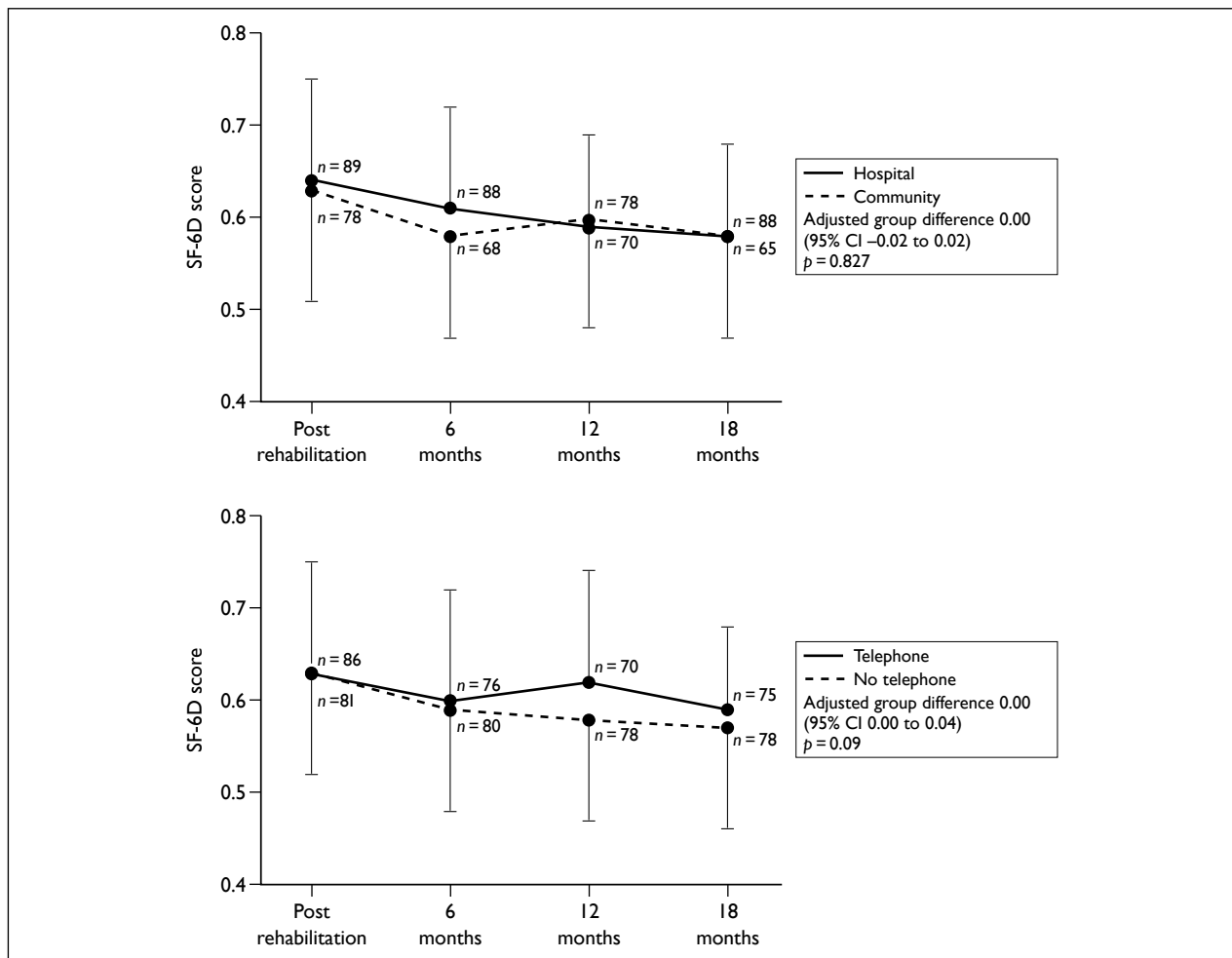
FIGURE 14 *SF-6D The figure shows the SF-6D, the summary parameter derived from the SF-36v2 generic health related quality of life measure, during follow-up. The upper panel shows hospital- vs community-treated groups, the lower shows telephone encouragement vs standard follow-up groups. Statistics refer to adjusted mean differences derived from ANCOVA as described in the text. (Data show means and standard deviations.)*
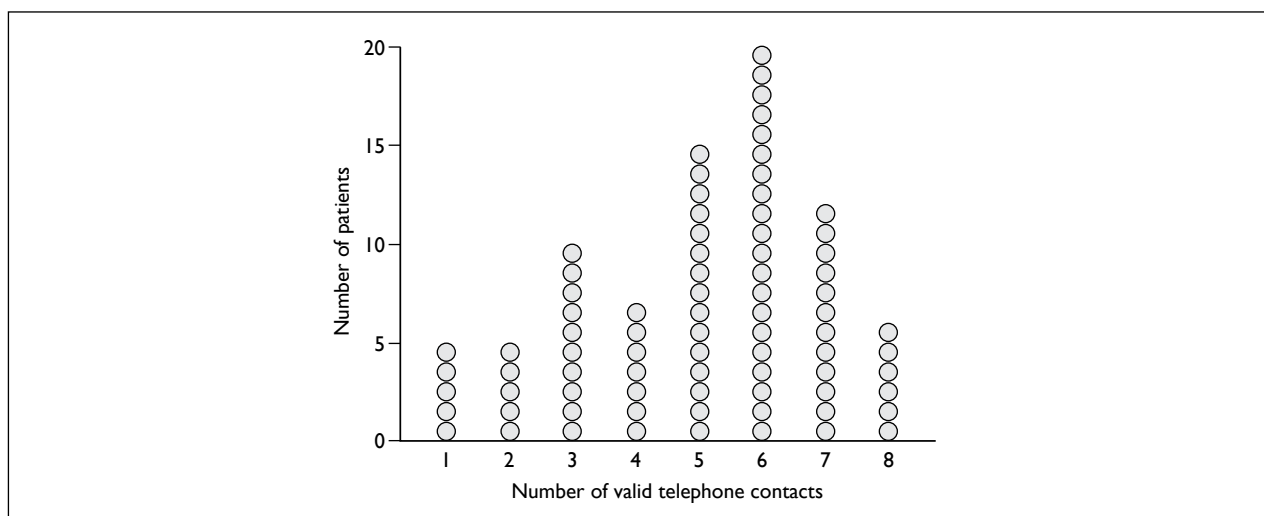
FIGURE 15 *Dot plot of number of valid telephone contacts (n = 80).*

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TABLE 34 *Details of telephone contacts*

	n	**Mean**	**Median**	**SD**	**Minimum**	**Maximum**
Number of valid telephone contacts	80	5.0	5.0	1.9	1.0	8.0
% of telephone calls in which patient reported still doing booklet exercises	80	61.0	66.7	33.4	0.0	100.0
% of telephone calls in which patient reported doing other exercises	80	69.4	71.4	25.6	0.0	100.0
% of telephone calls in which patient reported a medication change	80	17.1	0.0	24.4	0.0	100.0
% of telephone calls in which patient reported a GP contact	80	20.7	16.7	25.2	0.0	100.0
% of telephone calls in which patient reported new symptoms	80	18.7	0.0	26.6	0.0	100.0
% of telephone calls in which patient reported they felt better or same	80	64.7	69.0	31.0	0.0	100.0
% of telephone calls in which patient reported they felt better	80	21.4	12.5	26.8	0.0	100.0
% of telephone calls in which patient reported they felt worse	80	35.3	31.0	31.0	0.0	100.0
% of telephone calls in which patient reported increasing exercise time	80	10.4	0.0	17.1	0.0	62.5

Chapter 6
Economic analysis

Introduction

The use of pulmonary rehabilitation exercise programmes for people with COPD could have several important effects on costs and outcomes. The most obvious effect on costs might be a decrease in the demand for primary NHS services and costs associated with medication use, although an increase is also possible because of greater problem identification and referral. Increased demand on staff time for conducting the pulmonary rehabilitation sessions and the additional facilities hire and equipment costs have also to be measured. An economic evaluation was undertaken to capture these changes in resources and to evaluate cost-effectiveness.

Economic evaluation methods

The economic evaluation followed the technology appraisal guidelines used by NICE[26] and, as such, takes into account the NHS (rather than societal) perspective.

Outcomes of community and hospital pulmonary rehabilitation sessions were modelled as quality-adjusted life-years (QALYs), and costs measured in pound sterling. The comparative costs and outcomes of community and hospital pulmonary rehabilitation were estimated, along with the incremental cost per QALY of providing community pulmonary rehabilitation.

We perform a cost–utility analysis of pulmonary rehabilitation given in the routine (hospital) setting as opposed to the community setting. We also evaluate the effect of telephone follow-up calls on the long-term cost-effectiveness of pulmonary rehabilitation. Additionally assuming that individuals may not have the choice of location where they attend the pulmonary rehabilitation sessions, we assess the impact of follow-up calls where location is constrained.

Costs
Rehabilitation sessions

The cost of running an exercise programme includes staff time, facilities hire and equipment costs. Staff costs are based on the Department of Health 2003–4 national pay scales.[27] The Sheffield Teaching Hospitals NHS Foundation Trust finance department provided the equipment costs and the local rental costs for both the hospital- and the community-based pulmonary rehabilitation sessions.

In order to calculate the cost per session per individual of the pulmonary rehabilitation sessions, the equipment costs need to be converted into an equivalent annual cost (EAC). Based on expert opinion we estimated that up to 208 rehabilitation sessions can take place within a year. With a 4-year working life for the equipment and with the annuity charged at 3.5% and payable in advance, this translates to equipment costs of £1.76 per session. A portable oxygen cylinder has to be provided in the community setting at an annual cost of £121.73. This sum was divided over the 208 sessions that can take place over the year, and thus in the community setting the additional cost per session is £0.59. Equipment for nebulisation was treated similarly. Summing together the costs associated with the equipment, staff, facilities hire and travel costs (where relevant) allows us to arrive at a total cost per session. With eight individuals attending each pulmonary rehabilitation session, the cost per session per individual would amount to £28.67 and £33.14 for hospital and community pulmonary rehabilitation respectively.

Tables 35–37 (Appendix 1) present the costs associated with each intervention.

Other NHS services

The following items of resource use were identified:

- GP services
- district nurse visits

- health visitor visits
- social worker visits
- home help
- walk-in centre
- NHS Direct
- hospital visits
- prescriptions
- other NHS contacts.

Resource use data were collected via self-completion resource use questionnaires (asking individuals what resources they recall using over the previous 4 weeks) given to participants after randomisation to hospital or community pulmonary rehabilitation at baseline, then immediately post rehabilitation (8 weeks), and 6 months, 12 months and 18 months post intervention. At the end of the trial the NHS secondary care database for the city was queried to elicit hospital activity for each study participant. Outpatient, inpatient and accident and emergency (A&E) attendances were recorded.

The unit costs and drug costs used are shown in *Tables 38* and *39* respectively (Appendix 1). From the 2867 drug references collected from all individuals, we isolated the COPD-related prescriptions and linked these with the most common dosages in order to account for prescription costs in the most feasible manner. Individuals' resource usage was collected in intervals of 4 weeks over the five time periods during which questionnaires were completed. In order to reflect each individual's full resource usage in each of the different time periods, the 8-week, 6-month, 12-month and 18-month questionnaire responses were multiplied by two, four and six respectively (multiplied by six for both the 12-month and 18-month responses). These were then summed together to get the full 18-month resource usage per individual. The baseline drug and resource use data were excluded from the analysis as these data would not be affected by the subsequent allocation of individuals into the two treatment groups. Total costs were then aggregated across patients to derive a total cost per patient. This included the additional cost of providing hospital- or community-based pulmonary rehabilitation for all individuals randomised into each arm, prescription and resource usage costs. The analyses of the cost of follow-up telephone calls were added on to this in the analyses to follow.

Telephone follow-up calls

Individuals who were randomised to receive telephone follow-up calls were called by a member of the hospital research team following the pulmonary rehabilitation programme (in either setting) at 1, 2, 3, 4, 5, 6, 9, 12 and 15 months post rehabilitation. *Table 40* (Appendix 1) shows the details associated with the follow-up calls.

Outcomes

The SF-6D was calculated for all individuals at baseline, 8 weeks, 6 months, 12 months and 18 months post intervention. The SF-6D scores were estimated using the UK tariff.[28] The area under the curve (AUC) was calculated for individuals immediately post intervention up to 18 months. These were summed to arrive at the total QALY value for each individual over the 18-month period.

Analysis

The first comparison for the economic analysis was based on hospital- versus community-provided rehabilitation. A second analysis comparing routine follow-up with telephone follow-up in the hospital and community setting was also undertaken. This analysis evaluates whether telephone follow-up leads to prolonged benefits of pulmonary rehabilitation. In the final analyses, telephone follow-up is assessed where the setting is fixed to hospital or community in the delivery of the pulmonary rehabilitation sessions.

Although we found that both costs and effects were not statistically significantly different between setting or between routine and telephone follow-up, the costs and QALYs were combined in order to assess cost-effectiveness. This follows accepted practices in economic evaluation for handling decision uncertainty rather than relying on arbitrary rules of inference.[29,30] For the decision-maker, a *p*-value is insufficient to judge whether or not to fund a new service. What is more helpful is an estimate of the likelihood that a decision is going to be cost-effective. The main focus of the analysis is the plot data on the cost-effectiveness plane and their associated cost-effectiveness acceptability curves (CEACs). These plots were based on the bootstrapped sample means, generated from the cost–QALY pairs from the data. Interpretation of the CEAC was based around the probability of cost-effectiveness in the £20,000–30,000 per QALY range, which reflects the thresholds that are typically used by NICE to identify which interventions to fund.

A further set of analyses were undertaken to adjust the results for covariates in order to take into account differences in baseline characteristics and produce more accurate mean differences. Data were not imputed.

Results

Analysis of hospital versus community pulmonary rehabilitation at 18 months post rehabilitation

Analysis of cost-effectiveness is bivariate in nature and, in order to capture the covariance between costs and effects, is best undertaken on paired data (using cases where both cost and effects data are available). This requirement, together with the use of multiple data sources, typically leads to attrition. Of the 240 individuals who attended the baseline pre-rehabilitation assessment only 90 individuals provide full 18-month economic data.

For the sample of 90 cases of paired cost and effectiveness data at 18 months, *Table 41* (Appendix 1) shows the resource use items by study arm. There are no statistically significant differences in the number of resource use items in the two groups.

When combined with unit costs (see *Table 38*), the overall mean cost per individual (including the cost of hospital or community rehabilitation) was £4511.21 (£3794.69 SD) and £3643.74 (£3314.43 SD) for the hospital and community rehabilitation groups respectively.

From *Tables 41* and *42* (Appendix 1) we can see that the pulmonary rehabilitation sessions account for only a minority of the total costs (approximately 5%). Secondly, the difference in mean costs is largely determined by the differences in prescription costs.

The number of QALYs gained was greater in the hospital pulmonary rehabilitation group (*Table 43*), although not statistically significant. We find there that whilst costs are lower in the community group, outcomes are worse. However this does not take into account the sampling uncertainty associated with the costs and QALY pairs.

This uncertainty is best illustrated in the cost-effectiveness plane shown in *Figure 16*; at the centre of the cloud of points are the mean incremental cost and QALYs gained/lost for community-based

pulmonary rehabilitation from *Table 43* (Appendix 1) (–867.47 and –0.03) with a cost-effectiveness ratio of 28,819.75 (95% CI –270,737.45 to 35,905.61). This shows other combinations of costs and QALYs which are consistent with the data and produce sample means in all four quadrants (i.e. positive and negative costs and QALYs in every combination).

All this information can be summarised in the form of a CEAC, which is shown in *Figure 17*. This shows the probability that the intervention (community-based pulmonary rehabilitation) is cost-effective at various 'threshold values' of a QALY. If we are not willing to pay anything for an additional health gain, the intervention would have an 88% chance of being cost-effective; this reflects the fact that the majority of observations in *Figure 16* are in the south-west quadrant. In the range of willingness to pay for an additional QALY of £20,000–£30,000, the probability of the intervention being cost-effective decreases to between 56% and 50%. The fact that the scatter of points lies across all the quadrants in the scatter plot shows us that there is considerable uncertainty around the parameter estimates.

Costs were then adjusted using the following baseline data: resource use, gender and age. This resulted in the mean incremental cost saving associated with community pulmonary rehabilitation apparently reducing from £867 to £463, although in neither case was this a statistically significant difference. QALYs were adjusted using baseline utility and, again, age and gender. This had a negligible effect on the results, with no change in the incremental QALYs gained due to community pulmonary rehabilitation at the second decimal place. These adjustments result in diminishing the probability that community-based pulmonary rehabilitation is cost-effective.

Analysis of community versus hospital pulmonary rehabilitation with routine follow-up versus telephone follow-up

When we add the cost of follow-up telephone calls to the long-term (18-month) analysis we can see its impact on the long-term cost-effectiveness of pulmonary rehabilitation [*Table 44* (Appendix 1) and *Figure 18*].

We can see in *Figure 18* that the community-based pulmonary rehabilitation with telephone
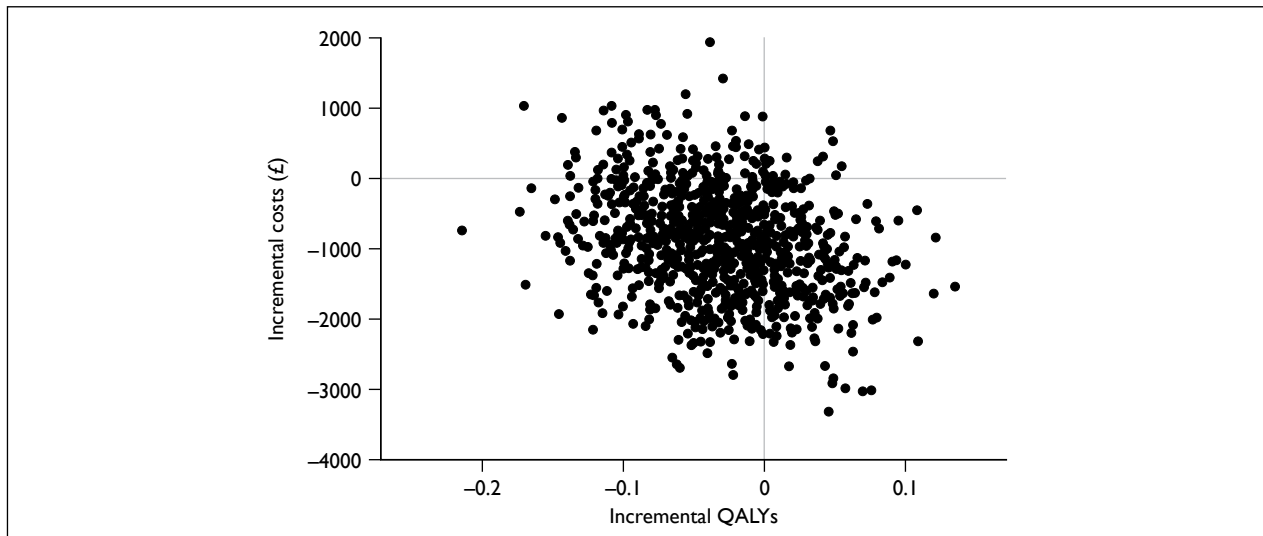
FIGURE 16 *Incremental costs and QALYs of community rehabilitation. The plot shows modelled estimates of the incremental cost difference for community vs hospital rehabilitation vs QALYs gained; for instance, plots to the lower left show models demonstrating a lower cost for community rehabilitation but a reduced gain in QALYs.*
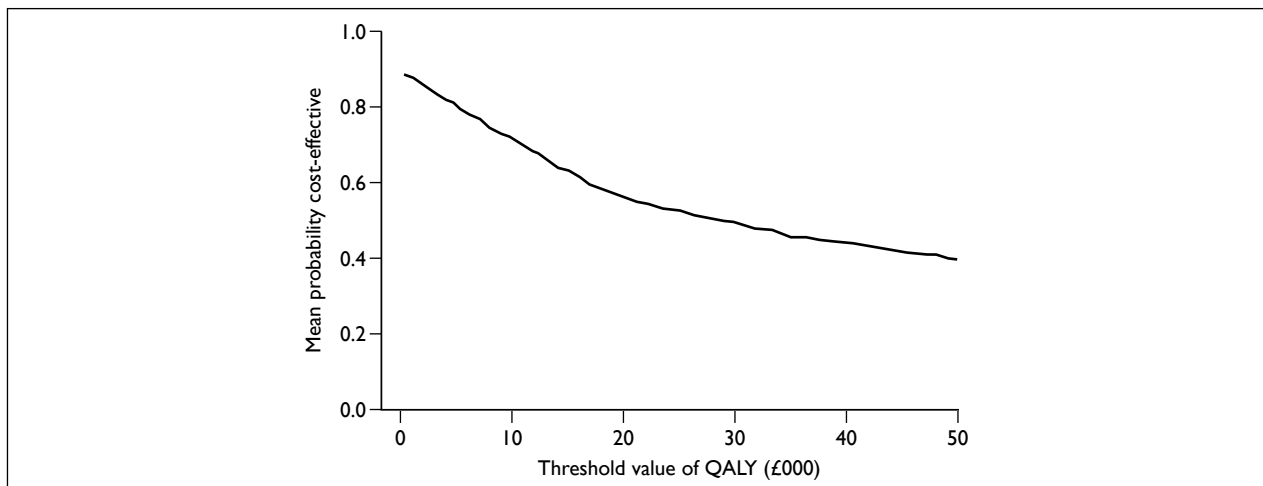
FIGURE 17 *Cost-effectiveness acceptability curve for community rehabilitation. The figure shows the probability that community-based pulmonary rehabilitation will be more cost-effective than hospital-based pulmonary for different threshold values of a QALY. Typically, NICE assumes a threshold value of a QALY as £10,000–20,000. The y-axis shows the probability that the new treatment is cost-effective.*

follow-up group is shown to be most likely to be cost-effective. The prolonged effects of telephone follow-up calls after pulmonary rehabilitation seem to have a greater impact on the community group as shown by comparing the difference between the two hospital curves, with standard and telephone follow-up with the community curves with standard and telephone follow-up. There is however significant uncertainty in this analysis.

Analysis routine follow-up versus telephone follow-up where the setting is fixed

An additional set of analyses were undertaken to assess the cost-effectiveness of telephone follow-up when the location of rehabilitation cannot be changed. In these circumstances the trial can provide information on the value of telephone follow-up (as this was randomised within each arm).
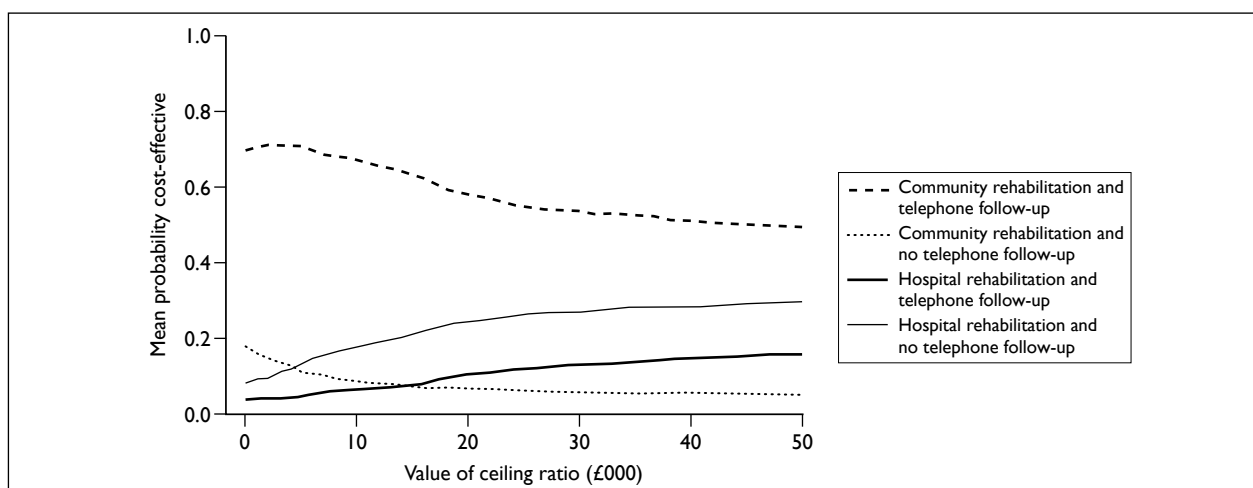
FIGURE 18 *Cost-effectiveness acceptability curves for four groups at 18 months. The figure shows the probability that each intervention group in the factorial design will prove most cost-effective for a threshold cost per QALY. NICE typically assumes a threshold cost per QALY of £10,000–20,000. The y-axis shows the proportion of simulations favouring each treatment.*
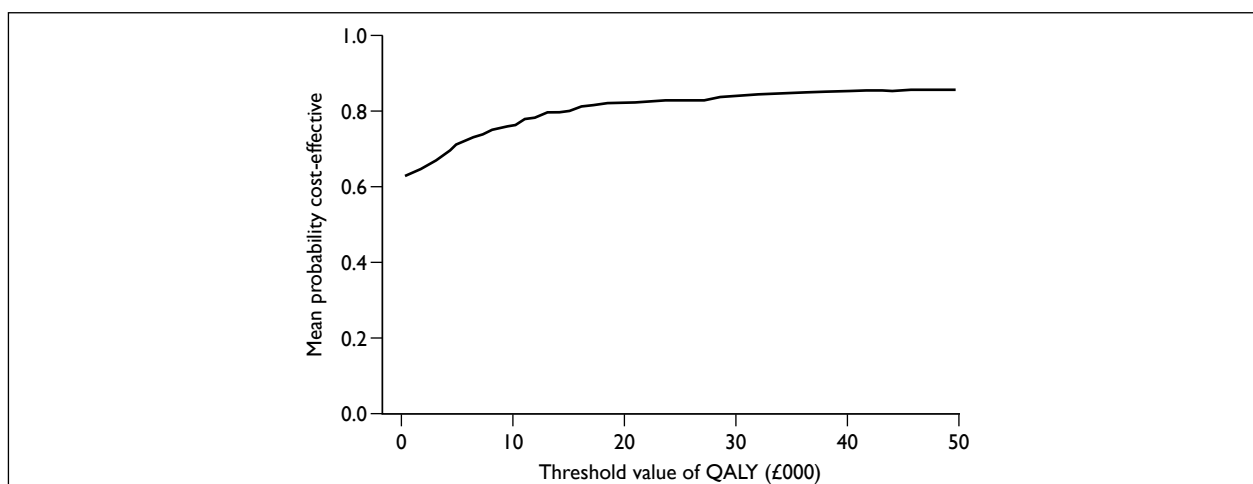
FIGURE 19 *Cost-effectiveness acceptability curves – routine vs telephone follow-up in the community group. The figure shows the corrected probability that telephone follow-up will be cost-effective compared with standard follow-up in the group receiving pulmonary rehabilitation in a community setting for various threshold costs per QALY. NICE typically assumes a threshold cost per QALY of £10,000–20,000. The y-axis shows the probability that the new treatment is cost-effective.*

Estimation of cost-effectiveness planes and CEACs indicate that, in the community setting, follow-up is cost-effective (87% chance at £20,000 per QALY), whilst hospital-based pulmonary rehabilitation follow-up is not cost-effective (31% chance at £20,000 per QALY). However, when each set of analyses are adjusted using the same baseline covariates as before, the results change (*Table 45*, Appendix 1). The changes are small for the community group, and consequently have a small impact on the associated CEAC; the probability of telephone follow-up being cost-effective at £20,000 per QALY reduces from 87% to 82% (*Figure 19*). However, the change for the hospital group is large, changing the probability of telephone follow-up being cost-effective at £20,000 per QALY from 31% to 72% (*Figure 20*).
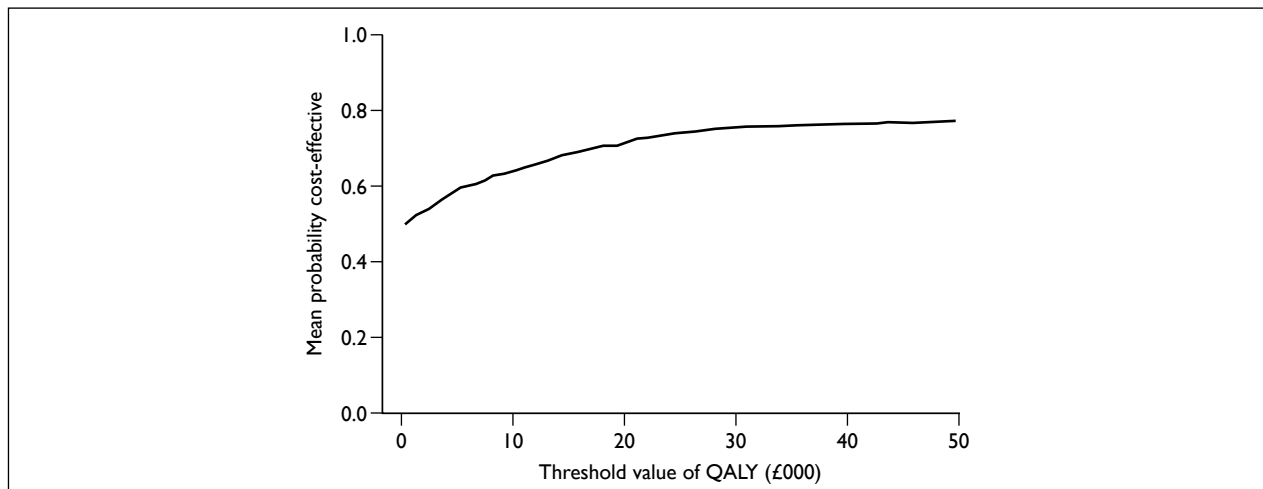
FIGURE 20 *Cost-effectiveness acceptability curves – routine vs telephone follow-up in the hospital group. The figure shows the corrected probability that telephone follow-up will be cost-effective compared with standard follow-up in the group receiving pulmonary rehabilitation in a community setting for various threshold costs per QALY. NICE typically assumes a threshold cost per QALY of £10,000–20,000. The y-axis shows the probability that the new treatment is cost-effective.*

Chapter 7
Discussion

This was a pragmatic trial to demonstrate whether, in routine clinical practice, pulmonary rehabilitation might be more effective, acutely or chronically, in a community setting than in secondary care settings. This was assessed in terms of both exercise capacity and generic and disease-specific health-care status measures. No significant difference was found between the venues of delivery. The trial also examined whether telephone follow-up might prolong the benefits of pulmonary rehabilitation compared with routine follow-up care. No significant difference was found in exercise capacity or HRQoL except that telephone follow-up seemed to produce benefit in the mastery and perhaps emotion domains of the CRQ. This led to a statistically significant but small improvement in overall CRQ score, although the mean improvement was small compared with the minimum important difference. Cost–utility analysis performed in the health economics evaluation shows significant uncertainty in the effectiveness of performing pulmonary rehabilitation in the community versus hospital setting. Thus, in practice, the balance of cost-effectiveness is likely to be determined by specific local factors such as the existing pattern of health-care provision, access and needs of a community rather than a more generalisable principle.

Lack of power and sample size

The primary outcome for the purposes of sample size estimation was the percentage change post rehabilitation relative to baseline (pre rehabilitation) in distance walked on the ESWT. Overall we had 161 (85 hospital and 76 community) patients with pre- and post-rehabilitation ESWT data for analysis. Clearly, we recruited fewer patients than the original sample size estimate of 186 patients per group (372 patients in total). This was based on a treatment effect of 100% and an estimated standard deviation of 343%. During their first meeting, the independent DMEC remarked on the relatively high SD used in this calculation, and suggested

that we recalculate the power of the study based on results of those patients studied to date (with blinding preserved). The revised sample calculation was scrutinised and accepted by the trial sponsors. A revised SD of 120% was estimated from the first 58 patients recruited to the trial. We also revised the MID effect downwards to a 60% difference. So, assuming an SD of 120%, if a difference in mean percentage change of 60% between the community and hospital groups is considered to be of clinical and practical importance, then to have an 80% power of detecting this difference in means as statistically significant at the 5% (two-sided) level would require 64 patients per group (128 in total). Using the revised SD of 120% and original effect size of 100%, with 70 patients per group, the study would have over 99% power to detect this difference as statistically significant at the 5% (two-sided) level if it really existed.

Sample size calculations were a priori because after we had carried out the study it was the observed data that determined the size and direction of the treatment effect and the width of any CI estimates for this treatment effect. The only parameter we needed to consider from the initial power calculation was the size of the effect we considered to be clinically meaningful, the MID, and how our observed treatment effect and associated CIs appear in relation to this MID. Statisticians have long faced the difficulty of trying to elicit the MID from researchers and clinicians, particularly for the objective of sample size calculations. Yet the same researchers, who find a difficulty in specifying a threshold for the MID a priori, often have no difficulty in doing so after the data have been collected and analysed and in declaring a post hoc result to be of clinical or practical importance or not. The concept of an a priori MID is not well defined. However, researchers should attempt to define the MID before the data are collected and analysed. If the MID is defined after the data are analysed then it is not meaningful. In summary, post hoc power calculations are not recommended. What investigators should do is calculate a CI for the observed treatment effect from the data collected. This CI should then be interpreted in

relation to the planned or minimum clinically relevant difference used in the initial sample size calculation. [31]

The actual standard deviation for the observed data turned out to be a little larger at 137% and 133% for the hospital and community rehabilitation groups respectively. Patients in the hospital rehabilitation group increased the distance they could walk at the post-rehabilitation follow-up by 283 m (SD 360 m), an increase relative to baseline of 109% (SD 137%). Patients in the community rehabilitation group increased the distance they could walk at the post-rehabilitation follow-up by 216 m (SD 340 m), an increase relative to baseline of 91% (SD 133%). The observed difference between the two groups in the change in distance walked relative to baseline was 17.8% (95% CI –24.3 to 59.9, $p = 0.405$, $n = 161$) in favour of hospital rehabilitation. However, the CI for this difference is wide, reflecting the sample size and the uncertainty in the outcome. The CI excludes the minimum we sought to examine in a priori power calculations. Hence, although there may be a small difference in outcome between the groups, if such a difference exists, it is smaller than the magnitude defined in our original power calculations or indeed in our revised more rigorous definition. Thus the study was in effect adequately powered though it failed to recruit as many participants as called for using the original power calculations. Overall the post-rehabilitation outcomes were broadly similar between the hospital and community rehabilitation groups, although we cannot say that they are absolutely equivalent.

Recruitment and selection

The major inclusion criterion was that patients should have MRC grade 3 breathlessness or worse that was predominantly due to COPD in the view of a respiratory physician, mirroring advice in the UK NICE guidelines. The trial was designed as a pragmatic or 'real world' trial and hence we tried to avoid overly prescriptive inclusion and exclusion clauses. Patients may have had modest degrees of additional heart failure, asthma or other diseases that contributed to their dyspnoea. We see this as a strength rather than a weakness, as it allows greater generalisability of data to the bulk of routine clinical practice rather than to a subset of patients.

Research participants were accepted from a variety of venues, including hospital outpatients, referral to physiotherapy and direct self-referral following

publicity. They were all reviewed by a respiratory physician to check the diagnosis and optimise treatment, unless such a review had already taken place within the last year. Diagnosis and treatment of COPD was in line with the GOLD guidelines.[14] Patients were included with stage 1 disease (i.e. FEV_1 in the normal range but an obstructive FEV_1/FVC ratio) if the physician felt COPD was the predominant cause of breathlessness. Hospital records for this subset of patients were reviewed, and patients included if there was clear radiological emphysema and a low gas transfer, with no alternative cause of dyspnoea apparent.

A maximal incremental shuttle test was included early in our assessment. We had some reservations about carrying out a maximal exercise test in a community setting without full resuscitation facilities, so these assessments were carried out in a hospital setting. In fact during the trial we did not experience significant side effects during these assessments. Further research on safety of maximal exercise testing in such patients would be valuable as it often forms part of rehabilitation protocols, and it would be useful to know the level of risk attached.

We felt that if no adverse events occurred during the initial maximal test, it would be safe to exercise patients in the community subsequently. The majority of exercise in the programme was performed at a submaximal level, and indeed was designed to be exercise that could be adopted as part of the patient's subsequent lifestyle.

In terms of pulmonary rehabilitation, this trial was large. The Cochrane Review of trials of pulmonary rehabilitation versus standard care[2] includes 30 trials with a mean of 42 ± 32 randomised study participants in total compared with 161 in this trial. After initial randomisation and before attendance for rehabilitation we found a large dropout. Again, this accords with previous findings. In the Cochrane Review, 84.8 ± 17.6% of those randomised were evaluated. Our trial produced evaluability broadly in line (67.5%) with these. No doubt some of the small trials reported could preferentially recruit highly motivated patients, so our data is in line with these findings.

One large trial of community versus hospital rehabilitation in Australia initially planned a significant follow-up phase but this was abandoned because of the low numbers of patients (27%) who could be successfully followed up.[32]

Clearly we too had a significant dropout rate during the trial, but we believe that the data are valuable in identifying the benefit that potentially can accrue in those followed up, and in quantitating and highlighting this important potential limitation to the widespread adoption of pulmonary rehabilitation in either setting. We do not report detailed qualitative data relating to the low uptake and follow-up, as these did not form part of the trial. However, for completeness, Appendix 4 includes a poster presentation of a small qualitative study performed whilst the participants in this trial attended follow-up sessions. Others have suggested that initial uptake is affected by enthusiasm of recruiting staff, particularly doctors,[33] as well as the accessibility of the programme and patients' perception of likely benefits.[34] Subsequently, a variety of factors affected adherence to the programme, such as problems related to the disease itself, and patients' expectations of treatment benefit and the limitations of their own disease.[35] Some authors have suggested that depressed patients may be less likely to attend.[36] External factors such as weather may also play a role.[37]

We believe that this is a point that has not been sufficiently emphasised and further research is needed. Whilst there is no doubt that pulmonary rehabilitation is effective and it is correctly recommended by NICE for widespread adoption, the large numbers of patients who are either unwilling or unable to take up the offer of a rehabilitation place, or who subsequently drop out, will by definition not benefit from this rehabilitation. Indeed, in population terms, measures taken to increase uptake of pulmonary rehabilitation overall will have much greater marginal benefit than fine tuning the details of the programme itself providing this adheres to accepted minimum standards. At the same time it should be noted that our data were treated as far as possible on an ITT analysis; all those with evaluable data were included as per their randomisation, whether or not they completed all the prescribed rehabilitation. Our data showed that the participants not returning after initial randomisation had no clear demographic differences from those who came back. There was a non-significant trend for non-attendees to be female and have lower MRC breathlessness scores. Perhaps these people perceived themselves as being less disabled, more active and/or less likely to benefit. Alternatively, it is known that women may place relatively low importance on their own health

maintenance, and tend to adopt a supportive role. Some of these relatively less disabled women may have concentrated on supporting other family members rather than seeing their own disease as a priority.[38]

Outcome measures

The co-primary outcome was the difference in improvement in ESWT between hospital and community pulmonary rehabilitation groups post rehabilitation, and the difference in ESWT during 18 months' follow-up between those receiving telephone encouragement and those receiving standard care. However, it has been reasonably argued that, as treatment of COPD is essentially symptomatic, health-care status outcomes might be more relevant.[2] We selected an exercise measurement as a clear and conventional outcome. Such outcomes are robust and easily compared between studies and with evaluation of other treatment modalities. As the core treatment modality is exercise training, it is logical to explore changes in exercise capacity as the direct effect of this. Licensing authorities continue to place reliance on physiological outcomes in trials of pharmacotherapy, for instance. We selected the ESWT as a well-validated tool to be sensitive to the effects of pulmonary rehabilitation.[12,13] The test is standardised in such a way as to tend towards isotime exercise at baseline to allow sensitivity to subsequent change. Time or distance might be reported as outcomes. Here we report both to allow full examination of data and definition of patient characteristics throughout follow-up. A problem with this measure is that there is not a clearly defined minimum important difference. We arbitrarily defined this a priori as a 100% change in time (as per the power calculations), subsequently adopting a more rigorous definition of 60%. Examination of the order of magnitude of change in ESWT time that was likely to lead to self-reporting of quality of life as 'better' rather than 'unchanged' or 'worse' suggests that this was justified (see Appendix 4).

Nevertheless, it is important to consider whether a change in exercise capacity translates to a change in health-care status, and to attempt to quantify that change. We used a variety of outcome measures. The SF-36 is a widely validated generic measure of HRQoL. The SF-6D extracted from version 2 is important as it allows calculation of cost-effectiveness by calculating QALYs.

We also utilised the CRQ, which as its name implies is a validated tool for use on inpatients with respiratory disease, and as such is more responsive to change than a generic tool.[39] Finally, we also collected EQ-5D data. There has been interest in using this very simple marker and we felt it a valuable inclusion as it might be easily incorporated into routine care to allow audit of effectiveness of programmes in the future.[42]

Safety

Current British Thoracic Society (BTS) guidelines[1] state:

> The prevalence of ischaemic heart disease in this population has not been well defined. The rate of critical incidents occurring during routine maximal exercise testing, even in patients with cardiac disease, is small. Modest physical exercise does not appear to produce myocardial repolarisation abnormalities, even in the presence of hypoxaemia, in patients with COPD. However, it is recommended that simple first aid medication (oxygen, nebulised bronchodilators, glyceryl trinitrin, etc.) should be available on site. Staff supervising exercise programmes should be trained in resuscitation (e.g. to Advanced Life Support (ALS) standard). The backup of a hospital arrest team is probably unnecessary.

We performed initial maximal ISWTs in a hospital setting because of a concern for safety. No adverse events were recorded during the exercise testing, although we empirically excluded anyone with desaturation to below 80% on pulse oximetry during this test, following discussion with our DMEC.

Patients were advised to take their medication to the rehabilitation sessions. We had no adverse events during rehabilitation that were thought to be attributable to the intervention. Further reporting of safety data from ongoing audit would be useful, in particular relating to the safety of maximal exercise testing and of such programmes in those with a requirement for long-term oxygen or who desaturate on exercise.

There are no clear recommendations regarding safety issues in the NICE commissioning guidelines for pulmonary rehabilitation.[40] The BTS's conclusion that hospital cardiac arrest teams are 'probably' not necessary suggests that further data on safety would be useful.

Acute effects

As noted, there was a significant dropout after randomisation but before initial pre-rehabilitation visit. It should be noted that the protocol utilised was identical in hospital and community to ensure that any differences observed were due to the setting per se. This meant that we did not use complex exercise devices such as exercise bicycles, treadmills or ergometers. Such a programme could easily be adopted in a very large range of settings and local circumstances. We considered our analysis to be ITT, but study participants were required to have evaluable pre-rehabilitation data to be included in the analysis. There was no significant difference in demographic characteristics between those who dropped out of the study before the pre-rehabilitation assessment and those who continued in the study either in community or hospital arms (except for the trend for women who were less symptomatic to drop out as noted above). We believe therefore that the results obtained in those evaluable data are likely to be generalisable. If those who declined rehabilitation in the current study could be encouraged to attend and participate in a rehabilitation programme, there is no a priori reason to suspect there would be a difference in outcome between them and the patients evaluated.

Overall efficacy

Using pooled data, the endurance shuttle walking time improved from 5.7 to 10.2 minutes. This approximately 80% improvement is of the same order as that reported by others.[13] Thus our simple protocol produced excellent improvements in exercise capacity.

Disease-specific quality of life assessed by CRQ improved significantly in total, and in all of its constituent domains of fatigue, dyspnoea, emotion and mastery. Improvements were of the order of 0.4 in each case. The minimal clinically important difference is around 0.5.[41] The 95% CI for improvement includes this value.

This accords with condition (a) in *Figure 5*, a statistically significant and potentially clinically important change, although there is uncertainty over whether the actual average improvement

truly exceeds the minimum important difference. These improvements were a little less than those included in the Cochrane Review of pulmonary rehabilitation.[2] There is no clear reason for the apparent discrepancy between the relatively large improvement in exercise capacity and the more modest improvement in CRQ compared with other studies. This may relate to the fact that we allowed our participants to self-fill their follow-up CRQs, although a published self-fill questionnaire appeared to have similar sensitivity and magnitude of change to the interviewer-led version.[41] It could also be because we collected HRQoL data before the participants performed the ESWT, and so were unaware of the magnitude of change in this measurement. More importantly, it may also relate to the fact that follow-up data on HRQoL were obtained where possible on those who did not complete or attend rehabilitation, treating this as an ITT analysis. This is likely to better reflect which health impacts might be expected in a population from a public health perspective and hence better inform decisions about service commissioning. As noted above, our trial was relatively large and inclusive. Possibly earlier, more selective trials recruited patients with more potential for improvement.

The generic HRQoL measures showed significant benefits with the exception of the EQ-5D. Although this showed a trend to benefit, it fell short of statistical significance. This is notable, as this measurement has been advanced as a simple and useful measure that might be used in cost-effectiveness calculations.[42] In total our results suggest that our programme produced worthwhile HRQoL benefits, but that the EQ-5D was less sensitive to these changes. We would caution against relying on it.

In conclusion, our pulmonary rehabilitation protocol was effective in producing benefits in exercise capacity, and quality of life as measured by disease-specific and generic tests.

Comparative result by site of rehabilitation – exercise capacity

There was no significant difference in improvement in patients in the hospital group, who increased their exercise time by 89.7%, compared with those in the community group, who improved by 76.2%. The CIs show the magnitude of any possible difference is small compared with the change produced by treatment at either venue.

Comparative result by site of rehabilitation – quality of life

Disease-specific (CRQ) and generic (SF-6D) quality of life measures improved statistically significantly after rehabilitation, although the simpler EQ-5D score was unable to reflect this. There was no difference between post-rehabilitation scores in community or hospital in terms of overall scores or different domains of the questionnaires. There was no trend apparent on inspection of the data, and this remained true when the data were corrected for pre-rehabilitation scores.

Physiotherapy team

We were interested to note a strong trend towards a differential effect depending on physiotherapy team, falling just short of conventional statistical significance. The same protocol delivered to indistinguishable research participants appeared to have differing absolute effects, independent of the site at which rehabilitation was carried out. The effect of this was potentially large, and could even be of the same order as the overall mean treatment effect of care delivered by several teams. We have not found any similar reports in the published work and, although this falls marginally short of accepted statistical significance and comes from a post hoc examination of data, it certainly merits further research.

Rehabilitation for those limited by a disabling disease may be a challenging process, and interpersonal relationships with therapists are likely to be important. If factors leading to success could be identified, this could guide selection and training of therapists in the future.

Summary of acute effects

A simple model of pulmonary rehabilitation produces worthwhile effects in terms of exercise capacity and generic and disease-specific measures of HRQoL. This is true whether it is provided in a hospital or a community setting. There was no significant difference between the effects in either setting. There was no clear evidence that one was significantly more likely to be cost-effective than the other.

Maintenance of effects

Inevitably, a number of patients did not complete the follow-up as intended. For comparison of

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hospital versus community outcomes, we included in analysis all patients who attended for pre-rehabilitation assessment whether or not complete data were subsequently available. If patients did not wish to attend the hospital for full testing, they were given the option of completing quality of life questionnaires at home, and missing data were extrapolated as described.

For analysis of telephone versus routine care, full data sets had to be available post rehabilitation. The analysis examined persistence of treatment effect by measuring change of exercise capacity and HRQoL from this point onwards.

As the study was a 2×2 factorial design, initial analysis included a test for interaction between the groups (hospital versus community, and telephone encouragement versus standard care). No such interaction of significance was found so we continued to analyse as in a factorial design.

Exercise capacity

As expected there was a progressive diminution of exercise capacity over the course of 18 months' follow-up.[43–50] There was however no difference in the rate of decline between groups receiving treatment in the community or in the hospital. There was no significant difference in persistence of effect in the group receiving telephone follow-up versus standard care. This remained true even when data were corrected for baseline (post-rehabilitation) time walked, time (follow-up visit) and factorial design, although there was a non-significant trend towards greater efficacy in the telephone follow-up group.

Data interpolation reduced any trend towards difference. This supports the contention that it is unlikely a real difference existed and was obscured by differential dropout from each study group.

Health-related quality of life

There was no difference in HRQoL over the 18 months of follow-up between those whose rehabilitation was received in community or hospital settings. This was the case with both generic and disease-specific HRQoL measures.

Telephone follow-up versus standard care produced no significant differences in HRQoL as measured by generic instruments. However, when the CRQ was used as a disease-specific HRQoL outcome, statistically significant differences were found.

There was a significant difference in favour of telephone follow-up overall. The overall effect size was small and did not exceed the minimum important difference.

Of the four domains that contribute to the total CRQ score, mastery was significantly enhanced. There was a trend to improvement in emotional scores, but fatigue and dyspnoea scores were not enhanced. The magnitude of effect was important. The minimum clinically significant difference for overall score is 2. We found a difference in mean total score of 0.92. This was more striking in the mastery domain, where the mean improvement of 0.4 was of the same order as the minimum clinically significant difference of 0.5, suggesting a greater number of individuals across a population might derive significant benefit.[41] This was in fact a similar magnitude to the change found before and after rehabilitation itself.

This makes intuitive sense in that telephone follow-up emphasising people's ability to have an impact on their own health through exercise could be expected to affect people's overall sense of mastery over their condition. One might also expect, if this were true, for there to be some emotional benefit and it is certainly interesting that there was a trend to improvement in this domain which would be coherent. This might not necessarily translate into an alteration in behaviour to produce enough change in exercise to result in a measurable effect on overall fitness. If this is the case then there may be no benefit on more physical outcomes such as exercise, fatigue and to a lesser extent dyspnoea.

The fact that the demonstrated significant effects are in a non-physical domain should not be dismissed lightly. Patients' behaviour and beliefs are bound to be important in affecting their interaction with health services.[8,51] It may well be important in modulating such things as unnecessary or unplanned health-care contacts, and forming the background to acceptance or otherwise of self-management programmes. The fact that a disease-specific quality of life measure appears more sensitive to change than a generic one is entirely to be expected from the nature of the instrument, and indeed is one of the main reasons that it was developed.

The improvements we have shown are modest, but we used a very simple model of follow-up which concentrated on encouragement to exercise rather than giving health advice in general. It was given in a scripted manner by individuals with a

relatively low level of general clinical training, such as assistant respiratory physiologists, and was brief. These findings certainly encourage exploration of whether the exact model of telephone contact could be improved to enhance its effects. It is possible that more clinical advice, longer telephone calls, or more frequent calls might give an even greater effect. In addition, our model of telephone contact involved extra calls by individuals not usually involved in the individual's usual clinical care. It is possible that by integration of the calls into existing follow-up by respiratory nurses, physiotherapists and general practitioners, the impact could also be increased, although the implications for costs are unclear. All these ideas deserve to be tested. It has been suggested that telephone encouragement to exercise alone may produce health gains in COPD even in the absence of a formal rehabilitation programme.[52] This was however an uncontrolled study that commenced with a 2-week home assessment that itself may have influenced outcomes, and recruited patients as soon as 2 weeks after an acute exacerbation. They would be expected to be improving their exercise capacity at this stage without any intervention.

One other study has looked at efficacy of telephone follow-up, although this was confounded by also including monthly personally supervised follow-up sessions as well as weekly telephone follow-up.[51] The study evaluated 190 patients completing pulmonary rehabilitation out of 340 initially recruited. The telephone intervention in that study was more wide ranging in scope than the one used in ours. In that study, there was better maintenance in improvement in exercise capacity as measured by 6-minute walk test, and in overall quality of life measured by the Quality of Well-Being Scale. However, as adjudged by the authors, the effects were small. There was no effect on change of overall CRQ. The component domains are not separately reported.

The reasons for the different findings are not clear. Ries *et al.*[51] report a group of patients, some of whom had diseases other than COPD. The study is from the US and it is possible that there is a different effect of telephone calls that is culturally based. A phone call is more likely to have impact if it is a relatively unusual event. We have no data to enable us to explore this further.

Some other studies examining post-rehabilitation maintenance treatment have used intensive follow-up strategies, such as 18 months of rehabilitation followed by twice-weekly rehabilitation, then either weekly or monthly supervised exercise.[53] These are

unlikely to be cost-effective unless producing very large effects. In this context, simple and cheap telephone follow-up demands further attention.

Economic evaluation

There have been relatively few other studies that examine the cost-effectiveness of pulmonary rehabilitation and the need for further studies is emphasised in the ERS/ATS guidelines.[6] The importance of critically examining cost-effectiveness is illustrated by the finding that intensive self-management plans (which are being increasingly adopted) may not in fact be cost-effective.[54] Given that long-term effects of pulmonary rehabilitation are likely to rely on behavioural changes with some overlap with self-management programmes, this urges caution.

The clearest data on the cost-effectiveness of pulmonary rehabilitation come from an RCT in the UK.[55] This showed that there was a clear but non-significant trend towards cost-effectiveness of pulmonary rehabilitation versus standard care and concluded that it was at least cost neutral.

A trial in the US suggested that rehabilitation could be cost-effective,[56] but this used comparison of data in the years before and after intervention rather than being an RCT. Information to date therefore suggests that pulmonary rehabilitation is cost-effective.

At 18 months, community-based pulmonary rehabilitation had a lower mean cost of £867 ($p > 0.05$) and produced 0.03 fewer QALYs ($p > 0.05$). When assessed in combination, the CEAC indicates that there is a 56% chance that community rehabilitation is cost-effective at £20,000 per QALY. When cost and QALY estimates are adjusted this figure reduces. In essence, the results show that both community and hospital rehabilitation have about a 50% chance of being cost-effective. This reflects both the small differences seen in outcomes and the large amount of variability seen in costs. The conclusion from these results is that service providers can choose which type of pulmonary rehabilitation service they feel is most appropriate for the skills and resources available, taking into account patient preferences.

Once the choice of setting has been made (or if a service has the setting forced upon them), the cost-effectiveness analysis suggests that telephone follow-up could be cost-effective. However, it should be noted that this is a secondary analysis

of the economic data, and the results are also dependent on adjustment for covariates. In practice, the uncertainty around this value does not allow firm conclusions to be reached. Further research is required.

Owing to the sick patient group, length of follow-up and the need for patient completed data for the economic analysis, attrition was high (61%). This makes the results highly uncertain. As discussed, imputation of data shows that a large effect on quality of life is unlikely to be concealed by differential dropout, supporting the relevancy of these analyses.

One further area of uncertainty is the longer term cost and health impacts of the two forms of rehabilitation and follow-up. If the treatment is expected to have an impact beyond 18 months, then further work would be necessary to model these impacts.

When acting on the results of this analysis, services need to consider their own costs, as they may vary from those used in this analysis. Especially in early stages, Trusts may be able to make use of spare capacity to run services well below the average costs given in *Table 37* (Appendix 1).

Limitations of this study

Patients were randomised to treatment groups, and analysis of the demographics of resulting groups shows that they were indeed well matched. However, there is no conceivable way to blind the treatment group either to research participants or to those carrying out treatment. Those supervising the rehabilitation programme did so for both randomisation groups to the same protocol, and they should have been identical. It is impossible to exclude some bias because of pre-existing views and prejudices about the differing study groups on the part of the therapists. The fact that outcomes were very similar suggests that this was unlikely to play a significant role. The use of separate treatment and assessment teams with the latter blinded to treatment sought to minimise bias in the assessment process itself.

The fact that patients would have an unblinded view is not relevant in this study. One of the significant factors that led to our performing the study was the hypothesis that patients might experience differing overall efficacy of a rehabilitation programme as a result of their differing preconceptions and perceptions. Any

'bias' caused by patient unblinding reflects the real effects in routine medical practice.

A major limitation of this study is the dropout rate between randomisation and initial assessment and subsequent dropout during the study. As discussed, our performance in these areas seems in line with other studies. This study was constructed as a pragmatic trial to examine practical ways to deliver care in health communities rather than in precisely examining a mechanistic hypothesis. The difficulty of recruitment and retention is a real clinical problem which must be addressed when planning future health-care delivery and predicting likely outcomes in terms of public health. This limits confidence in the data overall. However, we could not identify demographic or disease severity factors that predicted dropout, and data imputation produced more conservative results, i.e. it was less likely that significant differences existed between groups. Hence, our main conclusion of clinical similarity between groups is likely to remain valid despite this.

We excluded significantly hypoxaemic patients and did not provide oxygen for exercise. There is some evidence that oxygen provision during exercise may enhance the beneficial effect of pulmonary rehabilitation inpatients with COPD, although this is weak.[57] It remains a moot point as to whether it is reasonable to extend community provision to such hypoxic patients and whether a more complex programme requiring routine oxygen usage is reasonable. It might be argued that such patients are more safely and practically treated in a hospital setting but we have no data to address this.

Our analysis tried to be inclusive, so that we used all subjects with initial evaluable data on an ITT basis whether or not there were subsequent full data sets. This included continuing to collect HRQoL questionnaires from those refusing to attend the hospital for follow-up physiological measurements, and indeed to collect data for the long-term follow-up from people who had attended very few pulmonary rehabilitation treatment sessions.

Our major measure of exercise capacity, the ESWT is well validated and known to be sensitive to the change produced by pulmonary rehabilitation programmes. A drawback is the lack of clearly defined minimal clinically significant changes. However, the post-rehabilitation changes we witnessed overall were large and likely to be of significance. By contrast, even the extreme of the 95% CI for between-group difference was

considerably smaller, and was less than the a priori value we utilised as likely to be significant in our power calculations.

As noted above, we used a simple model of telephone follow-up. This was intentionally adopted as a very cheap and practical intervention that could be easily adopted if found to be effective. However, we do not know if more intensive telephone intervention might have produced greater effects.

This report uses health economic data that are based on patient recall of contact with health-care professionals. It uses a 'snapshot' reference period of 4 weeks before each assessment attendance. This is likely to be the source of some inaccuracy. However, this was supplemented by an analysis of hospital attendances derived from local hospital databases. Hospital contacts will be a major cost driver, so the inaccuracies of patient recall will be limited.

Qualitative data collection was not funded as part of the study and hence we do not report any data on perceptions of the programme and of patient preference. However, for completeness, Appendix 4 includes some qualitative data collected separately from our research participants.

Implications for health-care provision

This study showed that there is no clear reason to favour hospital or community provision of pulmonary rehabilitation for patients with COPD in terms of efficacy in improving exercise capacity or HRQoL. However, clear evidence is presented that group-based community rehabilitation is safe, effective and capable of producing results similar to hospital outpatient programmes.

Telephone follow-up produced beneficial long-term effects in terms of mastery. This selective effect on a component of HRQoL may be important but did not translate through to improvement on generic HRQoL scores (which would be expected to be less sensitive) overall. However, although the economic analysis suggested that telephone follow-up could be cost-effective at the threshold range operated by NICE, the data are not robust and do not permit a firm conclusion to be reached.

The evaluation showed similarity in the cost-effectiveness of community provision as opposed to hospital provision. In developing pulmonary rehabilitation services for a health community, careful attention to local factors that may impact on outcome is needed.

We have shown that a lot of people apparently suitable for group pulmonary rehabilitation are not willing to participate in it. Service providers should be aware of this and should ensure that services are as simple as possible to access. They should also try to offer alternative modes of management for those not accessing group rehabilitation services.

Implications for research

This study randomised people to a venue, then some of them had to wait a long time for the sessions to start. This is very similar to the delays between referral and treatment in some busy pulmonary rehabilitation centres. We found that many people changed their minds about whether they wanted to take part in group exercise sessions in that waiting period, or that the symptoms of their respiratory or a concomitant disease had worsened. These people were thus shown as dropouts before the trial had started. Most studies start with people at the inception of pulmonary rehabilitation sessions, which may give a distorted view of overall efficacy.

We have shown that there are many people who are suitable for pulmonary rehabilitation but decline to utilise the treatment. Further research is required on factors affecting uptake of pulmonary rehabilitation.

Our research concluded that community rehabilitation is safe. We excluded those on long-term oxygen therapy, those who had marked exertional hypoxaemia and those with cardiac failure (as well as other significant comorbidity). Additional research is required to assess the safety and efficacy of community programmes in these more complex patient groups.

Our data suggest that there could be an important difference in the magnitude of treatment effects that different teams can produce, even when working to a standard protocol. Further research is indicated to verify if this is true and, if so, what factors (e.g. interpersonal skills) are important.

We have shown that a simple form of telephone communication can affect mastery. Further research is required to evaluate costs and benefits in other aspects of symptom control and to the efficacy of differing forms of telephone follow-up.

Acknowledgements

Contribution of authors

Rod Lawson was the chief investigator. He prepared the submission documents then provided the majority of the medical input into the study. He was principal author of the report.

Judith Waterhouse was the study co-ordinator. She suggested the joint application to the HTA. On becoming the part time study co-ordinator she took day-to-day responsibility for all aspects of the study, organising the scheduling of the pulmonary rehabilitation sessions, training the data collection personnel and performing collection herself when necessary. She also helped create the text of the documents and proof read all submissions.

Stephen Walters was the study statistician. He was involved with the project at the design stage (including sample size calculation), prepared the randomisation schedule and continued as an active member of the steering group. He also performed the statistical analyses of the data and participated in the interpretation of the data and the writing (and revising) of the report (particularly the results chapter).

Yemi Oluboyede was the health-care economist. She came into the project when it was ongoing and analysed the economic data and wrote Chapter 6.

References

1. Chronic obstructive pulmonary disease: national clinical guideline on management of chronic obstructive pulmonary disease in adults in primary and secondary care. *Thorax* 2004;**59**(Suppl. 1):1–232.

2. Lacasse Y, Goldstein R, Lasserson TJ, Martin S. Pulmonary rehabilitation for chronic obstructive pulmonary disease. *Cochrane Database Syst Rev* 2006;**4**:CD00379.

3. Goldstein RS, Gort EH, Stubbing D, Avendano MA, Guyatt GH. Randomised controlled trial of respiratory rehabilitation. *Lancet* 1994;**344**:1394–7.

4. California Pulmonary Rehabilitation Collaborative Group. Effects of pulmonary rehabilitation on dyspnea, quality of life, and healthcare costs in California. *J Cardiopulm Rehabil* 2004;**24**:52–62.

5. Karapolat H, Atasever A, Atamaz F, Kirazli Y, Elmas F, Erdinc E. Do the benefits gained using a short-term pulmonary rehabilitation program remain in COPD patients after participation? *Lung* 2007;**185**:221–5.

6. Nici L, Donner C, Wouters E, Zuwallack R, Ambrosino N, Bourbeau J, *et al*. American Thoracic Society/European Respiratory Society statement on pulmonary rehabilitation. *Am J Respir Crit Care Med* 2006;**173**:1390–413.

7. Spruit MA, Troosters T, Trappenburg JC, Decramer M, Gosselink R. Exercise training during rehabilitation of patients with COPD: a current perspective. *Patient Educ Couns* 2004;**52**:243–8.

8. Schoo AM. A literature review of rehabilitative intervention for chronic obstructive pulmonary disease patients. *Aust Health Rev* 1997;**20**:120–32.

9. The Stationery Office. *Our health, our care, our say: a new direction for community services*. Norwich: Pbd TSO; 2006.

10. Foglio K, Bianchi L, Bruletti G, Porta R, Vitacca M, Balbi B, *et al*. Seven-year time course of lung function, symptoms, health-related quality of life, and exercise tolerance in COPD patients undergoing pulmonary rehabilitation programs. *Respir Med* 2007;**101**:1961–70.

11. Spencer LM, Alison JA, McKeough ZJ. Do supervised weekly exercise programs maintain functional exercise capacity and quality of life, twelve months after pulmonary rehabilitation in COPD? *BMC Pulm Med* 2007;**7**:7.

12. Revill SM, Morgan MD, Singh SJ, Williams J, Hardman AE. The endurance shuttle walk: a new field test for the assessment of endurance capacity in chronic obstructive pulmonary disease. *Thorax* 1999;**54**:213–22.

13. Eaton T, Young P, Nicol K, Kolbe J. The endurance shuttle walking test: a responsive measure in pulmonary rehabilitation for COPD patients. *Chron Respir Dis* 2006;**3**:3–9.

14. Pauwels RA, Buist AS, Ma P, Jenkins CR, Hurd SS; GOLD Scientific Committee. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: National Heart, Lung, and Blood Institute and World Health Organization Global Initiative for Chronic Obstructive Lung Disease (GOLD): executive summary. *Respir Care* 2001;**46**:798–825.

15. Fletcher CM, Elmes PC, Wood CH. The significance of respiratory symptoms and the diagnosis of chronic bronchitis in a working populations. *Br Med J* 1959;**1**:257–66.

16. StataCorp. *Stata Statistical Software: Release 9.0*. College Station, Texas: Stata Corporation; 2005.

17. ICH Harmonised Tripartite Guideline. *Statistical principles for clinical trials E9*. Current Step 4 version dated 5 February 1998.

18. Morley JE. *Undernutrition: Merck Manual Professional*. URL: www.merck.com/mmpe/sec01/ch002/ch002a.html (accessed September 2009).

19. Moher D, Schulz KF, Altman DG, for the CONSORT Group. The CONSORT statement: revised recommendations for improving the quality of reports of parallel-group randomised trials. *Lancet* 2001;**357**:1191–4.

20. Zwarenstein M, Treweek S, Gagnier JJ, Altman DG, Tunis S, Haynes B, *et al*. Improving the reporting of pragmatic trials: an extension of the CONSORT statement. *BMJ* 2008;**337**:a2390.

21. Frison L, Pocock SJ. Repeated measures in clinical trials: analysis using mean summary statistics and its implications for design. *Stat Med* 1992;**11**:1685–704.

22. Diggle PJ, Heagerty P, Liang K-Y, Zeger SL. *Analysis of longitudinal data*. 2nd edition. Oxford: Oxford University Press; 2002.

23. Campbell MJ, Machin D, Walters SJ. *Medical Statistics: A text book for the health sciences*. 4th edition. Chichester: Wiley; 2007.

24. Ware JE, Snow KK, Kosinski M, Gandek B. *SF-36 Health Survey Manual and Interpretation Guide*. Boston, MA: The Health Institute, New England Medical Centre; 1993.

25. Walters SJ, Brazier JE. Comparison of the minimally important difference for two health state utility measures: EQ-5D and SF-6D. *Qual Life Res* 2005;**14**:1523–32.

26. National Institute for Clinical Excellence. *Guide to the methods of technology appraisal*. London: NICE; 2004.

27. Curtis L, Netten A. *Unit costs of health and social care*. University of Kent, PSSRU: Kent; 2005.

28. Brazier JE, Roberts J, Deverill M. The estimation of a preference-based measure of health from the SF-36. *J Health Econ* 2002;**21**:271–92.

29. Claxton K. The irrelevance of inference: a decision making approach to the stochastic evaluation of health care technologies. *J Health Econ* 1999;**18**:341–64.

30. Drummond MF, Sculpher MJ, Torrance GW, O'Brien BJ, Stoddart GL. *Methods for the economic evaluation of health care programmes*. 3rd edition. Oxford: Oxford University Press; 2005.

31. Walters SJ. Consultants' forum: should post hoc sample size calculations be done? *Pharm Stat* 2009;**8**:163–9.

32. Elliott M, Watson C, Wilkinson E, Musk AW, Lake FR. Short- and long-term hospital and community exercise programmes for patients with chronic obstructive pulmonary disease. *Respirology* 2004;**9**:345–51.

33. Arnold E, Bruton A, Ellis-Hill C. Adherence to pulmonary rehabilitation: A qualitative study. *Respir Med* 2006;**100**:1716–23.

34. Taylor R, Dawson S, Roberts N, Sridhar M, Partridge MR. Why do patients decline to take part in a research project involving pulmonary rehabilitation? *Respir Med* 2007;**101**:1942–6.

35. Fischer MJ, Scharloo M, Abbink JJ, Thijs-Van A, Rudolphus A, Snoei L, *et al*. Participation and drop-out in pulmonary rehabilitation: a qualitative analysis of the patient's perspective. *Clin Rehabil* 2007;**21**:212–21.

36. Garrod R, Marshall J, Barley E, Jones PW. Predictors of success and failure in pulmonary rehabilitation. *Eur Respir J* 2006;**27**:788–94.

37. O'Shea SD, Taylor NF, Paratz JD. …But watch out for the weather: factors affecting adherence to progressive resistance exercise for persons with COPD. *J Cardiopulm Rehabil Prev* 2007;**27**:166–74.

38. Wuest J. Institutionalizing women's oppression: the inherent risk in health policy that fosters community participation. *Health Care Women Int* 1993;**14**:407–17.

39. Puhan MA, Guyatt GH, Goldstein R, Mador J, McKim D, Stahl E, *et al*. Relative responsiveness of the Chronic Respiratory Questionnaire, St. Georges Respiratory Questionnaire and four other health-related quality of life instruments for patients with chronic lung disease. *Respir Med* 2007 Feb;**101**:308–16.

40. NICE. *Pulmonary rehabilitation service for patients with COPD*. URL: http://www.nice.org.uk/usingguidance/commissioningguides/pulmonaryrehabilitationserviceforpatientswithcopd/pulmonaryrehabilitationservicecopd.jsp (accessed September 2009).

41. Williams JE, Singh SJ, Sewell L, Morgan MD. Health status measurement: sensitivity of the self-reported Chronic Respiratory Questionnaire (CRQ-SR) in pulmonary rehabilitation. *Thorax* 2003;**58**:515–8.

42. Rutten-van Mölken MP, Oostenbrink JB, Tashkin DP, Burkhart D, Monz BU. Does quality of life of COPD patients as measured by the generic EuroQol five-dimension questionnaire differentiate between COPD severity stages? *Chest* 2006;**130**:1117–28.

43. Spruit MA, Troosters T, Trappenburg JC, Decramer M, Gosselink R. Exercise training during rehabilitation of patients with COPD: a current perspective. *Patient Educ Couns* 2004;**52**:243–8.

44. Karapolat H, Atasever A, Atamaz F, Kirazli Y, Elmas F, Erdinc E. Do the benefits gained using a short-term pulmonary rehabilitation program remain in COPD patients after participation? *Lung* 2007;**185**:221–5.

45. Griffiths TL, Burr ML, Campbell IA, Lewis-Jenkins V, Mullins J, Shiels K, *et al*. Results at 1 year of outpatient multidisciplinary pulmonary rehabilitation: a randomised controlled trial. *Lancet* 2000;**355**:362–8.

46. Troosters T, Gosselink R, Decramer M. Short- and long-term effects of outpatient rehabilitation in patients with chronic obstructive pulmonary disease: a randomized trial. *Am J Med* 2000;**109**:207–212.

47. Strijbos JH, PostmaDS, van Altena R, Gimeno F, Koeter GH. A comparison between an outpatient hospital-based pulmonary rehabilitation program and a home-care pulmonary rehabilitation program in patients with COPD: a follow-up of 18 months. *Chest* 1996;**109**:366–372.

48. Engstrom CP, Persson LO, Larsson S, Sullivan M. Long-term effects of a pulmonary rehabilitation programme in outpatients with chronic obstructive pulmonary disease: a randomized controlled study. *Scand J Rehabil Med* 1999;**31**:207–13.

49. Foglio K, Bianchi L, Bruletti G, Battista L, Pagani M, Ambrosino N. Long-term effectiveness of pulmonary rehabilitation in patients with chronic airway obstruction. *Eur Respir J* 1999;**13**:125–32.

50. Vale F, Reardon JZ, ZuWallack RL. The long-term benefits of outpatient pulmonary rehabilitation on exercise endurance and quality of life. *Chest* 1993;**103**:42–5.

51. Ries AL, Kaplan RM, Myers R, Prewitt LM. Maintenance after pulmonary rehabilitation in chronic lung disease: a randomized trial. *Am J Respir Crit Care Med* 2003 Mar;**167**:880–8.

52. Wewel AR, Gellerman I, Schwerfege I, Morfeld M, Magnussen H, Jörres RA. Intervention by phone calls raises domiciliary activity and exercise capacity in patients with severe COPD. *Respir Med* 2008;**102**:20–6.

53. Wijkstra PJ, van Altena R, Krann J, Otten V, Postma DS, Koeter GH. Long term benefits of rehabilitation at home on quality of life and exercise tolerance in patients with chronic obstructive pulmonary disease. *Thorax* 1995;**50**:824–8.

54. Monninkhof E, van der Valk P, Schermer T, van der Palen J, van Herwaarden C, Zielhuis G. Economic evaluation of a comprehensive self-management programme in patients with moderate to severe chronic obstructive pulmonary disease. *Chron Respir Dis* 2004;**1**:7–16.

55. Griffiths TL, Phillips CJ, Davies S, Burr ML, Campbell IA. Cost effectiveness of an outpatient multidisciplinary pulmonary rehabilitation programme. *Thorax* 2001;**56**:779–84.

56. Golmohammadi K, Jacobs P, Sin DD. Economic evaluation of a community-based pulmonary rehabilitation program for chronic obstructive pulmonary disease. *Lung* 2004;**182**:187–96.

57. Nonoyama ML, Brooks D, Lacasse Y, Guyatt GH, Goldstein RS. Oxygen therapy during exercise training in chronic obstructive pulmonary disease. *Cochrane Database Syst Rev* 2007;**2**:CD005372.

Appendix 1

Supplementary tables

TABLE 35 *Staff costs*

	Description	Total time over 12 sessions (hours)	Costs per session (£)
Administration	Physiotherapist	24	70.00
	Physiotherapy assistant	24	21.60
Staffing for 12 pulmonary rehabilitation sessions	Physiotherapist	36	105.00
	Physiotherapy assistant	36	32.40
	Consultant	1	7.67
	Nurse G grade	1	3.92
	OT trust grade 10	2	6.66
	Dietician	1	2.42
	BreathEasy volunteer	1	1.75
Total cost per session			251.42

OT, occupational therapist.
Salaries are based on 2003–4 scales. For employers superannuation contributions at 11.8%.
Costed volunteer as a health-care assistant.

TABLE 36 *Equipment costs*

	Quantity	Purchase price (£)	Total cost (£)
Reebok step	1	39.00	39.00
Football	1	6.22	6.22
Medicine ball	1	17.12	17.12
Dumbells	2	9.95	19.90
Chair raises	1	32.95	32.95
Ankle/wrist weights	0.05 kg	11.50	11.50
	1 kg	14.50	14.50
Theraband 3 resistances	5.5 m light	6.50	6.50
	5.5 m medium	7.50	7.50
	5.5 m heavy	8.95	8.95
Swiffer	2	5.00	10.00
Unihoc puck	2	5.00	10.00
Washing line	1	1.00	1.00
Pegs	1 bag	1.00	1.00
Pillow cases	2	2.50	5.00
Weight for pillow cases (×2)	1 kg	5.93	5.93
	2 kg	8.63	8.63
Storage box	1	30	30.00
CD player	1	29.99	29.99
ISWT CD	2	16.50	33.00
Clipboards and pens	11	8.15	8.15
BP monitor	3	49.74	49.74
Saturation monitor	2	Saturation monitor – 310.00	620.00
	2	Finger probes – 168.00	336.00
Total cost			**1312.58**
Nebulizer	1	80.00	80.00
Portable O$_2$ cylinder	1	121.73 (annual cost)	121.73

CD, compact disc; ISWT, incremental shuttle walking test.

TABLE 37 *Total cost per session*

	Cost per session (£)	
	Hospital	**Community**
Staff	251.42	251.42
Facilities hire	10.00	27.92
Staff travel	0.00	17.25
Portable O$_2$ cylinder (121.73/208)	0.00	0.59
Nebuliser	0.00	0.40
Equipment EAC	1.75	1.75
Total cost per session	**263.17**	**299.33**
Total cost per attendance	**32.89**	**37.41**

EAC, equivalent annual cost.

TABLE 38 *Units costs used to value resource items*

	Unit cost (£)	Source
Telephone health advice (GP)	22	PSSRU 2005 (pp. 141 of 221) – per telephone consultation lasting 10.8 minutes
GP surgery consultations	20	PSSRU 2005 (pp. 141 of 221) – per surgery consultation lasting 10 minutes
GP home visits (assume 30 minutes)	96	PSSRU 2005 (pp. 141 of 221) – per home visit minute
Nurse home visits	19	PSSRU 2005 (pp. 133 of 221) – per home visit
Health visitor visits	28	PSSRU 2005 (pp. 135 of 221) – per home visit
Social worker visits	106	PSSRU 2005 (pp. 135 of 221) – per hour of face-to-face contact
Home help	14	PSSRU 2005 (pp. 149 of 221) – per hour face-to face weekday contact
Walk-in centre	39	Reference costs 2003/4, discrete MIU – per attendance 2004/05
NHS Direct	25	Hansard and Department of Health for call volume (6,427,321) and cost (161,900,000) respectively – cost per call 2004/05
A&E attendance (no investigation – referred/discharged)	62.41	HRG 04/05 – TA&E (V08 – General Medicine)
Inpatient	176–871	Trust financial returns 03/04 (see Appendix)
Outpatient	62–427	Trust financial returns 03/04 (see Appendix)

HRG, Healthcare Resource Groups (HRGs); MIU, minor injuries unit; PSSRU, Personal Social Services Research Unit; TA&E, National Schedule of Reference Costs – NHS Trusts Accident and Emergency (TA&E) HRG data.
PSSRU estimates were obtained from *Unit costs of health and social care*.

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TABLE 39 *Drug costs – COPD-related drugs only*

	Dosage	**Cost per dose (£)**
General		
Beclomethasone dipropionate	200 µg	0.21
Bendroflumethiazide	2.5 mg	0.04
Budesonide	200 µg	0.31
Budesonide with formoterol	1 dose	0.63
Carbocisteine	375 mg	0.28
Co-amilofruse	1 tablet	0.05
Combivent	1 dose	0.06
Fluticasone propionate with salmeterol	1 dose	1.22
Ipratropium bromide MDI	20 µg	0.04
Ipratropium bromide nebuliser solution	250 µg	0.68
Prednisolone	5 mg	0.05
Quinine bisulphate	300 mg	0.08
Salbutamol	100 µg	0.03
Salmeterol	25 µg	0.49
Terbutaline	500 µg	0.14
Theophylline SR	250–500 mg	0.68
Tiotropium	18 µg	1.25
		Cost per blister + device (£)
Fluticasone propionate		12.06
Antibiotics – assume 7-day course		
Amoxicillin	250 mg	0.06
Exacerbations		**Cost per exacerbation**
Prednisolone for 7 days	40 mg	3.15
Amoxicillin for 7 days	250 mg	

MDI, metered dose inhaler; SR, slow release.

TABLE 40 *Telephone follow up calls – cost per individual*

	Time taken (minutes)	**Total cost**
Staff costs[a]		
Administration	5	0.90
Call time	2.5	0.45
Call cost[b]		
Call duration	2.5	0.30
Total	10	1.65
Total cost for nine follow-up calls	90	14.85

a Physiotherapy assistant making calls – cost per minute of client contact = £0.18.
b British Telecom call charge per minute = £0.12.

TABLE 41 *Resource use by study arm (at 18 months)*

	Hospital rehabilitation (*n* = 47) Mean (SD)	Community rehabilitation (*n* = 43) Mean (SD)	Difference	95% CI of the difference	
				Lower	Upper
GP phone	4.55 (9.39)	2.19 (5.55)	2.37	–0.84	5.57
GP surgery	18.77 (13.59)	17.67 (11.39)	1.09	–4.19	6.37
GP home visit	2.13 (5.10)	1.44 (3.91)	0.69	–1.23	2.60
Walk-in centre	0.26 (0.90)	0.56 (2.10)	–0.30	–1.00	0.39
NHS Direct	0.17 (0.92)	0.28 (1.29)	–0.11	–0.57	0.35
District nurse visits	1.36 (5.01)	1.44 (4.46)	–0.08	–2.07	1.91
Health visitor visits	0.26 (1.75)	0.14 (0.91)	0.12	–0.46	0.70
Social worker visits	0.17 (0.82)	0.14 (0.91)	0.03	–0.33	0.39
Home help	2.81 (17.55)	10.70 (40.43)	–7.90	–21.26	5.48
Other services	1.53 (7.21)	2.19 (4.18)	–0.65	–3.11	1.80
PR sessions	9.17 (3.33)	9.88 (2.51)	–0.71	–1.96	0.53
Prescriptions	13.96 (6.24)	12.84 (5.23)	1.12	–1.30	3.54
OP/A&E attendances	7.28 (7.50)	6.17 (7.95)	1.14	–2.32	4.52
Inpatient days	3.14 (2.32)	2.05 (1.40)	1.09	–0.9	2.27

OP, outpatient; PR, pulmonary rehabilitation.

TABLE 42 *Costs by study arm (at 18 months)*

	Hospital rehabilitation (*n* = 47) Mean (SD)	Community rehabilitation (*n* = 43) Mean (SD)	Difference	95% CI of the difference	
				Lower	Upper
GP phone	91.06 (187.75)	43.72 (111.03)	47.34	–16.79	111.47
GP surgery	337.79 (244.69)	318.14 (205.00)	19.65	–75.39	114.68
GP home visit	178.72 (428.18)	121.12 (328.57)	57.61	–103.38	218.59
Walk-in centre	9.96 (34.95)	21.77 (82.21)	–11.81	–38.92	15.30
NHS Direct	4.26 (22.91)	7.00 (31.96)	–2.72	–14.30	8.86
District nurse visits	25.87 (95.12)	27.40 (84.70)	–1.52	–39.39	36.34
Health visitor visits	7.15 (49.01)	3.91 (25.62)	3.24	–13.00	19.49
Social worker visits	18.04 (86.51)	14.80 (97.00)	3.25	–35.19	41.69
Home help	39.32 (245.74)	149.77 (565.96)	–110.45	–297.64	76.75
Other services	54.43 (286.33)	42.05 (195.30)	12.38	–89.67	114.43
Average total per individual	755.98 (796.91)	739.36 (813.67)	16.63	–320.94	354.20
Prescription costs	1752.77 (2254.94)	928.32 (1119.26)	824.45	67.73	1581.16
PR sessions	262.91 (95.34)	327.55 (86.15)	–64.94	–102.27	–27.01
OP/A&E costs	727.59 (967.77)	650.69 (934.84)	76.90	–322.42	476.22
Inpatient costs	1011.96 (2493.00)	997.83 (2066.68)	14.13	–950.17	978.44
Average total for all resources per Individual	4511.21 (3794.69)	3643.74 (3314.43)	867.47	–631.17	2366.1125

OP, outpatient; PR, pulmonary rehabilitation.

TABLE 43 Costs and QALYs at 18 months post rehabilitation

	Hospital (*n*=47) Mean (SD)	Community (*n*=43) Mean (SD)	Mean difference	95% CI of the difference
Quality-adjusted life-years	1.54 (0.23)	1.51 (0.25)	–0.03	–0.13 to 0.07
Total costs	4511.21 (3794.69)	3643.74 (3314.43)	–867.47	–2366.11 to 631.17

TABLE 44 Outcomes at 18 months post rehabilitation with routine vs telephone follow-up

	Community-based PR with telephone follow-up (*n*=18) Mean (SD)	Community-based PR with standard follow-up (*n*=25) Mean (SD)	Hospital-based PR with telephone follow-up (*n*=23) Mean (SD)	Hospital -based PR with standard follow-up (*n*=24) Mean (SD)
QALY	1.55 (0.24)	1.48 (0.26)	1.54 (0.25)	1.55 (0.21)
Total cost	3229.96 (3034.75)	3952.35 (3530.43)	4832.46 (4565.60)	4217.58 (2945.69)
PR, pulmonary rehabilitation.				

TABLE 45 Crude and adjusted incremental costs and QALYs of telephone follow-up for the pulmonary rehabilitation (PR) settings

	Crude		Adjusted	
	Mean incremental cost of follow-up (£)	Mean incremental QALYs with follow-up	Mean incremental cost of follow-up (£)	Mean incremental QALYs with follow-up
Hospital PR	+614	–0.01	+23	+0.04
Community PR	–722	+0.07	–223	+0.05

TABLE 46 *Sheffield Teaching Hospitals NHS Foundation Trust Costs 2003–4*

	Cost per bed day (£)	**Cost per outpatient attendance (£)**
Cardiology	515	107
Cardiothoracic	871	169
Clinical immunology & allergy	707	219
Dental specialties	628	77
Dermatology	269	73
Ear, nose and throat	647	85
Gastroenterology	316	113
General practice	356	142
General surgery	401	104
Genito-urinary medicine	262	158
Geriatrics	176	162
Gynaecology	489	100
Haematology	463	103
Infectious diseases	320	427
Medical oncology	440	177
Nephrology	323	125
Neurology	379	183
Neuro-surgery	606	184
Obstetrics	429	88
Ophthalmology	672	62
Orthopaedics	429	92
Other medicine	225	140
Paediatric surgery	574	130
Paediatrics	497	158
Plastic surgery	588	74
Rehabilitation medicine	209	279
Rheumatology	372	124
Thoracic medicine	259	153
Urology	369	90

2003–4 Sheffield Teaching Hospitals NHS Foundation Trust financial returns. Where a specialty does not exist, assigned 'other medicine' or 'general surgery' as appropriate.

Appendix 2

Questionnaires used

Appendix 2.1

Used at visit 1 in the 2 weeks prior to treatment.

A RANDOMISED **2X2** TRIAL OF COMMUNITY VERSUS HOSPITAL REHABILITATION, FOLLOWED BY TELEPHONE OR CONVENTIONAL FOLLOW UP; IMPACT ON QUALITY OF LIFE, EXERCISE CAPACITY AND USE OF HEALTHCARE RESOURCES

CoHoRT Study

Case Report Form

Patient ID

Date of Questionnaire

Pre Rehab

Also need MRC Breathlessness (blue), SF36 (lemon), EQ5D (green), CRQ(cream), Resource Use and Socioeconomic (pink)

Check Data

Subject initials   ☐☐☐

Date of Birth   ☐☐/☐☐/☐☐

Hosp no   ☐☐☐☐☐☐

North/South   Delete one

ID number from database   ☐☐☐☐

Inclusion criteria

Diagnosis of COPD	Yes/no
MRC grade 3 dyspnoea	Yes/no
Informed consent	Yes/no
Access to telephone number ☐☐☐☐ ☐☐☐ ☐☐☐☐	Yes/no
Willing/motivated to make lifestyle changes	Yes/no
Can hear and understand	Yes/no
Prognosis not under 2 years from any disease	Yes/no
No requirement for oxygen therapy	Yes/no
Stable or controlled cardiac disease	Yes/no
No musculoskeletal problems precluding exercise	Yes/no

(OR ATTACH CLINIC PROFORMA)

Patients GP

Has the subject had any exacerbations requiring a change in usual respiratory treatment in the last 4

weeks   Yes/no

If yes outcome is to return to waiting list on database

Bronchodilator
Give 2 puffs Salbutamol and/or 2 puffs Atrovent Forte

via Volumatic (10 tidal breath technique) time   ☐☐:☐☐

Incremental Shuttle test

Level walked   ☐☐

Distance walked in metres   ☐☐☐

Estimated VO2 max in ml/min/Kg   ☐☐.☐

[4.19+(0.025*distance walked)]

85% of VO2 max for endurance walk in ml/min/Kg   ☐☐.☐

[Estimated VO2 max*0.85]

Endurance shuttle level calculated   ☐☐

Starting SpO2	
Lowest SpO2	
Starting Heart Rate	
Highest Heart Rate	

Worksheet for Incremental Walk

(Strike through each 10 m length performed)

1	2	3							
4	5	6	7						
8	9	10	11	12					
13	14	15	16	17	18				
19	20	21	22	23	24	25			
26	27	28	29	30	31	32	33		
34	35	36	37	38	39	40	41	42	
43	44	45	46	47	48	49	50	51	52

Height and weight

Height in metres   □.□□

Weight in Kg   □□□.□

Mid upper arm muscle circumference

Distance to mid point in mm   □□□

Mid upper arm circumference in mm   □□□

Triceps skin fold thickness in mm   □□.□

Calculated mid upper arm muscle circumference *(calculated by database)*

First Questionnaires

Give subject SF36 to complete ☐ when completed

Give Resource use questionnaire to complete ☐ when completed

Give MRC Breathlessness to complete ☐ when completed

Spirometry

Perform spirometry at least 30 mins post bronchodilator

Circle bronchodilator/s   Atrovent   Salbutamol

Time of starting spirometry   ☐☐:☐☐

Relaxed Vital Capacity		
FEV$_1$		
FVC		
PEF		

Current Medication

medication	route	number	frequency

Second questionnaires

Interviewer filled CRQ   ☐ when completed

Self fill Eq5D   ☐ when completed

Endurance walk

Level set ☐☐

Distance walked in metres ☐☐☐☐

How long was the walk in minutes ☐☐.☐☐m

Was the walk stopped because level too low   Yes/No

If so increase by 2 levels and recommence

Starting SpO2	
Lowest SpO2	
Starting Heart Rate	
Highest Heart Rate	

Worksheet for Endurance Walk

(Strike through each 10 m length performed)

1	2	3	4	5	6	7	8	9	10
11	12	13	14	15	16	17	18	19	20
21	22	23	24	25	26	27	28	29	30
31	32	33	34	35	36	37	38	39	40
41	42	43	44	45	46	47	48	49	50
51	52	53	54	55	56	57	58	59	60
61	62	63	64	65	66	67	68	69	70
71	72	73	74	75	76	77	78	79	80
81	82	83	84	85	86	87	88	89	90
91	92	93	94	95	96	97	98	99	100

A RANDOMISED **2x2** TRIAL OF COMMUNITY VERSUS HOSPITAL REHABILITATION, FOLLOWED BY TELEPHONE OR CONVENTIONAL FOLLOW UP; IMPACT ON QUALITY OF LIFE, EXERCISE CAPACITY AND USE OF HEALTHCARE RESOURCES

CoHoRT Study

EQ-5D

Patient ID

Date of Questionnaire

✓ for timepoint	
	Pre Rehab
	Post Rehab
	Rehab plus 6 months
	Rehab plus 12 months
	Rehab plus 18 months
	Withdrawal from study

EUROQOL© HEALTH QUESTIONNAIRE

Here are some simple questions about your health in general. By ticking one answer in each group below, please indicate which statements best describe your own health state TODAY.

(Please circle <u>one</u> number)

1.   **Mobility**

   I have no problems in walking about   1

   I have some problems in walking about   2

   I am confined to bed   3

2.   **Self-care**

   I have no problems with self-care   1

   I have some problems washing or dressing myself   2

   I am unable to wash or dress myself   3

3.   **Usual Activities**

   I have no problems with performing my usual activities   1
   (e.g. work, study, housework, family or leisure activities)
   I have some problems with performing my usual activities   2

   I am unable to perform my usual activities   3

4.   **Pain/Discomfort**

   I have no pain or discomfort   1

   I have moderate pain or discomfort   2

   I have extreme pain or discomfort   3

5.   **Anxiety/Depression**

   I am not anxious or depressed   1

   I am moderately anxious or depressed   2

   I am extremely anxious or depressed   3

Please turn the page and continue

6. To help people say how good or bad their health is, we have drawn a scale (rather like a thermometer) on which the **best state** you can imagine is marked by **100** and the **worst state** you can imagine is marked by **0**.

We would like you to indicate on this scale how good or bad **your own health is today**, in your opinion. Please do this by drawing a line from the box below to whichever point on the scale indicates how good or bad **your current health state** is.

> **Your own health state today**

Best imaginable health state

```
100
 ┬
 ┼
 ┤
9 0
 ┼
 ┤
8 0
 ┼
 ┤
7 0
 ┼
 ┤
6 0
 ┼
 ┤
5 0
 ┼
 ┤
4 0
 ┼
 ┤
3 0
 ┼
 ┤
2 0
 ┼
 ┤
1 0
 ┼
 ┤
 0
```

Worst imaginable health state

THANK YOU FOR FILLING IN THIS QUESTIONNAIRE.

A RANDOMISED **2X2** TRIAL OF COMMUNITY VERSUS HOSPITAL REHABILITATION, FOLLOWED BY TELEPHONE OR CONVENTIONAL FOLLOW UP; IMPACT ON QUALITY OF LIFE, EXERCISE CAPACITY AND USE OF HEALTHCARE RESOURCES

CoHoRT Study

SF-36 v2

Patient ID

Date of Questionnaire

✓ for timepoint	
	Pre Rehab
	Post Rehab
	Rehab plus 6 months
	Rehab plus 12 months
	Rehab plus 18 months
	Withdrawal from study

HEALTH STATUS QUESTIONNAIRE

The following questions ask you about your health, how you feel and how well you are able to do your usual activities.

If you are unsure how to answer a question, please give the best answer you can.

OVERALL HEALTH

1.   <u>In general</u>, would you say your health is:

(Please circle <u>one</u> number only)

Excellent 1
Very good......................2
Good.............................3
Fair...............................4
Poor 5

2.   **Compared to <u>one year ago</u>, how would you rate your health in general <u>now</u>?**

(Please circle <u>one</u> number only)

Much better now than one year ago **1**
Somewhat better now than one year ago......... **2**
About the same as one year ago....................... **3**
Somewhat worse now than one year ago......... **4**
Much worse now than one year ago **5**

Please turn the page and continue

HEALTH AND DAILY ACTIVITIES

3. The following questions are about activities you might do during a typical day. Does <u>your health now limit you</u> in these activities? If so, how much?

(Please circle <u>one number on each line</u>)

ACTIVITIES	Yes, limited a lot	Yes, limited a little	No, not limited at all
a. Feeding yourself	1	2	3
b. Getting up from a chair	1	2	3
c. Bathing or dressing yourself	1	2	3
d. Walking in your home	1	2	3
e. Walking 100 yards	1	2	3
f. Walking half a mile	1	2	3
g. Walking more than a mile	1	2	3
h. Bending, kneeling or stooping	1	2	3
i. Climbing one flight of stairs	1	2	3
j. Climbing several flights of stairs	1	2	3
k. Lifting or carrying groceries	1	2	3
l. **Moderate** activities, such as moving a table, pushing a vacuum cleaner, bowling or playing golf	1	2	3
m. **Vigorous activities**, such as running, lifting heavy objects, participating in strenuous sports	1	2	3

4. During the <u>past 4 weeks</u>, how much of the time have you had any of the following problems with your work or other regular daily activities <u>as a result of your physical health</u>?

(Please circle <u>one number on each line</u>)

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a. Cut down on the **amount of time** you spent on work or other activities	1	2	3	4	5
b. **Accomplished less** than you would like	1	2	3	4	5
c. Were limited in the **kind** of work or other activities	1	2	3	4	5
d. Had **difficulty** performing the work or other activities (for example, it took extra effort)	1	2	3	4	5

5. During the <u>past 4 weeks</u>, how much of the time have you had any of the following problems with your work or other regular daily activities <u>as a result of any emotional problems</u> (such as feeling depressed or anxious)?

(Please circle <u>one number on each line</u>)

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a. Cut down on the **amount of time** you spent on work or other activities	1	2	3	4	5
b. **Accomplished less** than you would like	1	2	3	4	5
c. Did work or other activities **less carefully than usual**	1	2	3	4	5

6. During the <u>past 4 weeks</u>, to what extent have your physical health or emotional problems interfered with your normal social activities with family, friends, neighbours or groups?

(Please circle <u>one</u> number)

Not at all 1
Slightly............................ 2
Moderately 3
Quite a bit...................... 4
Extremely 5

7. How much <u>bodily</u> pain have you had during <u>the past 4 weeks</u>?

(Please circle <u>one</u> number)

None.............................. 1
Very mild 2
Mild................................ 3
Moderate 4
Severe............................ 5
Very severe 6

8. During the <u>past 4 weeks</u>, how much did <u>pain</u> interfere with your normal work (including both work outside the home and housework)?

(Please circle <u>one</u> number)

Not at all 1
A little bit........................ 2
Moderately 3
Quite a bit...................... 4
Extremely 5

Please turn the page and continue

YOUR FEELINGS

9. These questions are about how you feel and how things have been with you during <u>the past 4 weeks</u>. (For each question, please give the one answer that comes closest to the way you have been feeling.)

(Please <u>circle one number on each line</u>)

How much of the time during the <u>past 4 weeks</u>:	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a. Did you feel full of life?	1	2	3	4	5
b. Have you been very nervous?	1	2	3	4	5
c. Have you felt so down in the dumps that nothing could cheer you up?	1	2	3	4	5
d. Have you felt calm and peaceful?	1	2	3	4	5
e. Did you have a lot of energy?	1	2	3	4	5
f. Have you felt down-hearted and depressed?	1	2	3	4	5
g. Did you feel worn-out?	1	2	3	4	5
h. Have you been happy?	1	2	3	4	5
i. Did you feel tired?	1	2	3	4	5

Please turn the page and continue

HEALTH IN GENERAL

10. **During the <u>past 4 weeks</u>, how much of the time has your <u>physical health or emotional</u> problems interfered with your social activities (like visiting friends, relatives etc.)?**

(Please circle <u>one</u> number)

All of the time 1
Most of the time..............2
Some of the time............3
A little of the time............4
None of the time............5

11. **How TRUE or FALSE is <u>each</u> of the following statements for you?**

(Please circle <u>one number on each line</u>)

	Definitely true	Mostly true	Don't know	Mostly false	Definitely false
a. I seem to get ill more easily than other people	1	2	3	4	5
b. I am as healthy as anybody I know	1	2	3	4	5
c. I expect my health to get worse	1	2	3	4	5
d. My health is excellent	1	2	3	4	5

A RANDOMISED 2X2 TRIAL OF COMMUNITY VERSUS HOSPITAL REHABILITATION, FOLLOWED BY TELEPHONE OR CONVENTIONAL FOLLOW UP; IMPACT ON QUALITY OF LIFE, EXERCISE CAPACITY AND USE OF HEALTHCARE RESOURCES

CoHoRT Study

Resource Use and Socio-economic Questions

Patient ID

Date of Questionnaire

Pre Rehabilitation

| Q1 | What is your sex? | Male ☐ |
| | | Female ☐ |

| Q2 | What is your date of birth? | __ __ / __ __ / 19 __ __ |

Q3	What is your marital status? *(please tick one box)*	Single (never married) ☐
		Married (first marriage) ☐
		Re-married ☐
		Separated (but still legally married) ☐
		Divorced ☐
		Widowed ☐

Q4	What is your ethnic group? *(please tick one box)*	**White**
		British ☐
		Irish ☐
		Any other White background ☐
		*(please write in)*_____
		Mixed
		White and Black Caribbean ☐
		White and Black African
		White and Asian ☐
		Any other Mixed background ☐
		_____
		Continued on next page, please turn over

		Asian or Asian British	☐
		Indian	☐
		Pakistani	☐
		Bangladeshi	☐
		Any other Asian background	
		_____	
		(please write in)	
		Black or Black British	☐
		Caribbean	☐
		African	☐
		Any other Black background	
		_____	
		(please write in)	
		Chinese or other ethnic group	☐
		Chinese	☐
		_____	
		Any other	
		(please write in)	
Q5	What type of accommodation does your household occupy? *(please tick <u>one</u> box)*	**A whole house or bungalow that is:**	
		Detached	☐
		Semi – detached	☐
		Terraced (including end-terrace)	☐
		A flat, maisonette, or apartment	☐

Q6	Does your household own or rent the accommodation? *(please tick <u>one</u> box)*	Owns Outright	☐
		Owns with a mortgage or loan	☐
		Pays part rent and part mortgage (shared ownership)	☐
		Rents	☐
		Lives here rent free	☐
Q7	Does your accommodation have central heating?	Yes, in some or all rooms	☐
		No	☐
Q8	How many cars or vans are owned, or available for use, by one or more members of your household?	0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 or more ☐	
Q9	Do you do any work as an Employee, or on a Government sponsored training scheme, as self-employed/freelance, or in your own/family business?	Yes, full time ☐ *(please go to Q11)*	
		Yes, part time ☐ *(please go to Q11)*	
		No ☐ *(please go to Q10)*	

Q10	If NO, are you	Retired?	☐
		Student?	☐
		Looking after home/family?	☐
		Permanently sick/disabled?	☐
		None of the above?	☐
		(please go to Q12)	
Q11	If you are in paid employment, how many days have you had off work in the last month on account of your health?	_____ days	
Q12	Please could you tell me **how many times** you have used any of the following services in the last month.	GP telephone advice	☐
		GP surgery consultations	☐
		GP home visits	☐
		Walk in centre	☐
		NHS Direct	☐
		District nurse visits	☐
		Health visitor visits	☐
		Social worker visits	☐
		Hospital	☐
		Home help	☐
		Any other professional visitor or service (Please specify) _____	☐

Q13	Do you receive help with your daily Activities from a relative or friend?	Yes No	☐ ☐	*Go to Q14* *End of questionnaire*
Q14	If YES, on average, how much time per day/per week do they spend? **Now please go to Q15**	———————— hours per day ———————— days per week		
Q15	What would that person have been doing as their main activity if they had not been helping and/or caring for you?	Housework Childcare Caring for a relative or friend Voluntary work Leisure activities Attending school or university On sick leave Paid work Other (please specify)	☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐	
	If you answer to this question is paid work, please go to Q16, otherwise stop here.			
Q16	What is your carer's occupation?	————————————		

THANK YOU VERY MUCH FOR TAKING THE TIME TO COMPLETE THIS QUESTIONNAIRE.

We would like you to tell us something about your breathlessness over the last 24 hours. If you don't do something because you are too breathless to even think of doing it please ✓ "Yes"

As soon as you ✓ "No" in the shaded grey area you may stop answering questions.

		Yes	No
1	Are you short of breath on strenuous exercise?		
2	Are you short of breath when hurrying on the level or walking up slight hills		
3	Does shortness of breath make you walk slower than most people of your age on the flat Or Have you had to stop for breath after a mile or so (or after 15 minutes) on the level at your own pace due to shortness of breath		
4	Have you been stopping for breath after walking 100 yards (or after 4 minutes) on the level at your own pace		
5	Have you got short of breath after walking a few yards at your own pace Or Did getting undressed last night make you short of breath		

Appendix 2.2

Used at visit 2 in the week immediately post treatment.

Also used at visits 3, 4 and 5 (6-monthly intervals post treatment).

The EQ-5D and SF-36 version 2 are identical to those used at visit 1 and thus are not repeated here.

A RANDOMISED **2x2** TRIAL OF COMMUNITY VERSUS HOSPITAL REHABILITATION, FOLLOWED BY TELEPHONE OR CONVENTIONAL FOLLOW UP; IMPACT ON QUALITY OF LIFE, EXERCISE CAPACITY AND USE OF HEALTHCARE RESOURCES

CoHoRT Study

Case Report Form

Patient ID

Date of Questionnaire

✓ for timepoint	
	Post Rehab
	Rehab plus 6 months
	Rehab plus 12 months
	Rehab plus 18 months
	Withdrawal from study

Also need SF36 (lemon), EQ5D (green), CRQ (peach), Resource Use (lilac) and Global (gold)

Check Data

Subject initials ☐☐☐

Date of Birth ☐☐/☐☐/☐☐

ID number from database ☐☐☐☐

Patients GP

Bronchodilator
Give 2 puffs Salbutamol and/or 2 puffs Atrovent Forte

via Volumatic (10 tidal breath technique) time ☐☐:☐☐

Weight ☐☐☐.☐

Mid upper arm muscle circumference

Distance to mid point in mm ☐☐☐

Mid upper arm circumference in mm ☐☐☐

Triceps skin fold thickness in mm ☐☐

Calculated mid upper arm muscle circumference *(calculated by database)*

First Questionnaires

Give subject SF36 to complete ☐ when completed

Give Resource use questionnaire to complete ☐ when completed

Spirometry

Perform spirometry at least 30 mins post bronchodilator

Circle bronchodilator/s   Atrovent   Salbutamol

Time of starting spirometry   ☐☐:☐☐

Relaxed Vital Capacity		
FEV$_1$		
FVC		
PEF		

Medication Changes

Have you altered the dose you take of any medication   Yes/no

Changed dose medication	New route	New number	New frequency

Have you started any new medication   Yes/no

New medication	route	number	frequency

Have you stopped any medication   Yes/no

Discontinued medication	route	number	frequency

In the last year how many additional courses of treatment for your chest (antibiotics and/or steroids) have you needed

0   ❏

1-3   ❏

4-6

❏

over 6

❏

Second questionnaires

Self fill CRQ   ❏ when completed

Self fill Eq5D   ❏ when completed

Global health change   ❏ when completed

Endurance walk

Level set at first visit   ❏❏

Distance walked in metres   ❏❏❏❏

How long was the walk in minutes   ❏❏.❏❏m

Was the walk stopped at 20 mins   Yes/No

Starting SpO2	
Lowest SpO2	
Starting Heart Rate	
Highest Heart Rate	

Worksheet for Endurance Walk

(Strike through each 10 m length performed)

1	2	3	4	5	6	7	8	9	10
11	12	13	14	15	16	17	18	19	20
21	22	23	24	25	26	27	28	29	30
31	32	33	34	35	36	37	38	39	40
41	42	43	44	45	46	47	48	49	50
51	52	53	54	55	56	57	58	59	60
61	62	63	64	65	66	67	68	69	70
71	72	73	74	75	76	77	78	79	80
81	82	83	84	85	86	87	88	89	90
91	92	93	94	95	96	97	98	99	100

A RANDOMISED **2x2** TRIAL OF COMMUNITY VERSUS HOSPITAL REHABILITATION, FOLLOWED BY TELEPHONE OR CONVENTIONAL FOLLOW UP; IMPACT ON QUALITY OF LIFE, EXERCISE CAPACITY AND USE OF HEALTHCARE RESOURCES

CoHoRT Study

CRQ

Patient ID

Date of Questionnaire

✓ for timepoint	
	Post Rehab
	Rehab plus 6 months
	Rehab plus 12 months
	Rehab plus 18 months
	Withdrawal from study

CHRONIC RESPIRATORY QUESTIONNAIRE
FOLLOW UP

This is the questionnaire designed to find out how you have been feeling during the last 2 weeks. You will be asked about how short of breath you have been, how you have been feeling and how your mood has been.

The first time we did the questionnaire you thought of the activities you had done during the last two weeks that had made you short of breath, then you selected the five most important activities that had made you short of breath. These were *(list these from database)*

A	
B	
C	
D	
E	

We are going to continue to use those five activities in this questionnaire.

Please circle the appropriate number for each answer

Question 4

A   I would now like you to describe how much shortness of breath you have experienced during the last two weeks whilst

(repeat item from above)

1. EXTREMELY SHORT OF BREATH
2. VERY SHORT OF BREATH
3. QUITE A BIT SHORT OF BREATH
4. MODERATE SHORTNESS OF BREATH
5. SOME SHORTNESS OF BREATH
6. A LITTLE SHORTNESS OF BREATH
7. NOT AT ALL SHORT OF BREATH

B   I would now like you to describe how much shortness of breath you have experienced during the last two weeks whilst

(repeat item from above)

1. EXTREMELY SHORT OF BREATH
2. VERY SHORT OF BREATH
3. QUITE A BIT SHORT OF BREATH
4. MODERATE SHORTNESS OF BREATH
5. SOME SHORTNESS OF BREATH
6. A LITTLE SHORTNESS OF BREATH
7. NOT AT ALL SHORT OF BREATH

C   I would now like you to describe how much shortness of breath you have experienced during the last two weeks whilst

(repeat item from above)

1. EXTREMELY SHORT OF BREATH
2. VERY SHORT OF BREATH
3. QUITE A BIT SHORT OF BREATH
4. MODERATE SHORTNESS OF BREATH
5. SOME SHORTNESS OF BREATH
6. A LITTLE SHORTNESS OF BREATH
7. NOT AT ALL SHORT OF BREATH

D   I would now like you to describe how much shortness of breath you have experienced during the last two weeks whilst

(repeat item from above)

1. EXTREMELY SHORT OF BREATH
2. VERY SHORT OF BREATH
3. QUITE A BIT SHORT OF BREATH
4. MODERATE SHORTNESS OF BREATH
5. SOME SHORTNESS OF BREATH
6. A LITTLE SHORTNESS OF BREATH
7. NOT AT ALL SHORT OF BREATH

E   I would now like you to describe how much shortness of breath you have experienced during the last two weeks whilst

(repeat item from above)

1. EXTREMELY SHORT OF BREATH
2. VERY SHORT OF BREATH
3. QUITE A BIT SHORT OF BREATH
4. MODERATE SHORTNESS OF BREATH
5. SOME SHORTNESS OF BREATH
6. A LITTLE SHORTNESS OF BREATH
7. NOT AT ALL SHORT OF BREATH

Question 5

In general, how much of the time during the last two weeks have you felt frustrated or impatient?

1. ALL OF THE TIME
2. MOST OF THE TIME
3. A GOOD BIT OF THE TIME
4. SOME OF THE TIME
5. A LITTLE OF THE TIME
6. HARDLY ANY OF THE TIME
7. NONE OF THE TIME

Question 6

How often during the last two weeks did you have a feeling of fear or panic when you had difficulty getting your breath?

1. ALL OF THE TIME
2. MOST OF THE TIME
3. A GOOD BIT OF THE TIME
4. SOME OF THE TIME
5. A LITTLE OF THE TIME
6. HARDLY ANY OF THE TIME
7. NONE OF THE TIME

Question 7

What about fatigue? How tired have you felt over the last two weeks ?

1. EXTREMELY TIRED
2. VERY TIRED
3. QUITE A BIT TIRED
4. MODERATELY TIRED
5. SOMEWHAT TIRED
6. A LITTLE TIRED
7. NOT AT ALL TIRED

Question 8

How often during the last two weeks have you felt embarrassed by your coughing or heavy breathing?

1. ALL OF THE TIME
2. MOST OF THE TIME
3. A GOOD BIT OF THE TIME
4. SOME OF THE TIME
5. A LITTLE OF THE TIME
6. HARDLY ANY OF THE TIME
7. NONE OF THE TIME

Question 9

In the last two weeks how much of the time did you feel very confident and sure that you could deal with your illness?

1. NONE OF THE TIME
2. A LITTLE OF THE TIME
3. SOME OF THE TIME
4. A GOOD BIT OF THE TIME
5. MOST OF THE TIME
6. ALMOST ALL OF THE TIME
7. ALL OF THE TIME

Question 10

How much energy have you had in the last two weeks?

1. NO ENERGY AT ALL
2. A LITTLE ENERGY
3. SOME ENERGY
4. MODERATELY ENERGETIC
5. QUITE A BIT OF ENERGY
6. VERY ENERGETIC
7. FULL OF ENERGY

Question 11

In general, how much of the time did you feel upset, worried or depressed during the last two weeks?

1. ALL OF THE TIME
2. MOST OF THE TIME
3. A GOOD BIT OF THE TIME
4. SOME OF THE TIME
5. A LITTLE OF THE TIME
6. HARDLY ANY OF THE TIME
7. NONE OF THE TIME

Question 12

How often during the last two weeks did you feel that you had complete control of your breathing?

1. NONE OF THE TIME
2. A LITTLE OF THE TIME
3. SOME OF THE TIME
4. A GOOD BIT OF THE TIME
5. MOST OF THE TIME
6. ALMOST ALL OF THE TIME
7. ALL OF THE TIME

Question 13

How much of the time during the last two weeks did you feel relaxed and free of tension?

1. NONE OF THE TIME
2. A LITTLE OF THE TIME
3. SOME OF THE TIME
4. A GOOD BIT OF THE TIME
5. MOST OF THE TIME
6. ALMOST ALL OF THE TIME
7. ALL OF THE TIME

Question 14

How often during the last two weeks have you felt low in energy?

1. ALL OF THE TIME
2. MOST OF THE TIME
3. A GOOD BIT OF THE TIME
4. SOME OF THE TIME
5. A LITTLE OF THE TIME
6. HARDLY ANY OF THE TIME
7. NONE OF THE TIME

Question 15

In general, how often during the last two weeks have you felt discouraged or down in the dumps?

1. ALL OF THE TIME
2. MOST OF THE TIME
3. A GOOD BIT OF THE TIME
4. SOME OF THE TIME
5. A LITTLE OF THE TIME
6. HARDLY ANY OF THE TIME
7. NONE OF THE TIME

Question 16

How often during the last two weeks have you felt worn out or sluggish?

1. ALL OF THE TIME
2. MOST OF THE TIME
3. A GOOD BIT OF THE TIME
4. SOME OF THE TIME
5. A LITTLE OF THE TIME
6. HARDLY ANY OF THE TIME
7. NONE OF THE TIME

Question 17

How happy, satisfied or pleased have you felt with your personal life during the last two weeks?

1. VERY DISSATISFIED, UNHAPPY MOST OF THE TIME
2. GENERALLY DISSATISFIED, UNHAPPY
3. SOMEWHAT DISSATISFIED, UNHAPPY
4. GENERALLY SATISFIED, PLEASED
5. HAPPY MOST OF THE TIME
6. VERY HAPPY MOST OF THE TIME
7. EXTREMELY HAPPY, COULD NOT BE MORE SATISFIED OR PLEASED

Question 18

How often during the last two weeks did you feel upset or scared when you had difficulty getting your breath?

1. ALL OF THE TIME
2. MOST OF THE TIME
3. A GOOD BIT OF THE TIME
4. SOME OF THE TIME
5. A LITTLE OF THE TIME
6. HARDLY ANY OF THE TIME
7. NONE OF THE TIME

Question 19

In general, how often during the last two weeks have you felt restless, tense or uptight?

1. ALL OF THE TIME
2. MOST OF THE TIME
3. A GOOD BIT OF THE TIME
4. SOME OF THE TIME
5. A LITTLE OF THE TIME
6. HARDLY ANY OF THE TIME
7. NONE OF THE TIME

A RANDOMISED 2x2 TRIAL OF COMMUNITY VERSUS HOSPITAL REHABILITATION, FOLLOWED BY TELEPHONE OR CONVENTIONAL FOLLOW UP; IMPACT ON QUALITY OF LIFE, EXERCISE CAPACITY AND USE OF HEALTHCARE RESOURCES

CoHoRT Study

Resource Use

Patient ID

Date of Questionnaire

✓ *for timepoint*	
	Post Rehab
	Rehab plus 6 months
	Rehab plus 12 months
	Rehab plus 18 months
	Withdrawal from study

Q1	If you are in paid employment, how many days have you had off work in the last month on account of your health?	_____ days
Q2	Please could you tell me **how many times** you have used any of the following services in the last month.	GP telephone advice ☐
		GP surgery consultations ☐
		GP home visits ☐
		Walk in centre ☐
		NHS Direct ☐
		District nurse visits ☐
		Health visitor visits ☐
		Social worker visits ☐
		Hospital ☐
		Home help ☐
		Any other professional visitor or service ☐
		Please specify _____
Q3	In the last month have you received help with your daily activities from a relative or friend?	Yes ☐ Go to Q14
		No ☐ End of questionnaire
Q4	If YES, on average, how much time per day/per week do they spend?	_____ hours per day
		_____ days per week

Q5	What would that person have been doing as their main activity if they had not been helping and/or caring for you?	Housework	☐
		Childcare	☐
		Caring for a relative or friend	☐
		Voluntary work	☐
		Leisure activities	☐
		Attending school or university	☐
		On sick leave	☐
		Paid work	☐
		Other (please specify)	☐
		_____	
	If your answer to this question is paid work, please go to Q6, otherwise stop here.		
Q6	What is your carer's occupation?	_____	

THANK YOU VERY MUCH FOR TAKING THE TIME TO COMPLETE THIS QUESTIONNAIRE.

A RANDOMISED 2x2 TRIAL OF COMMUNITY VERSUS HOSPITAL REHABILITATION, FOLLOWED BY TELEPHONE OR CONVENTIONAL FOLLOW UP; IMPACT ON QUALITY OF LIFE, EXERCISE CAPACITY AND USE OF HEALTHCARE RESOURCES

CoHoRT Study

✓ for timepoint	
	Pre Rehab
	Post Rehab
	Rehab plus 6 months
	Rehab plus 12 months
	Rehab plus 18 months
	Withdrawal from study

Addressograph label

Global rating of health change question (v3)

Since the last time you saw us, has there been any change in your overall health-related quality of life?

Has your overall health-related quality of life been:

(Please circle <u>one</u> number only)

1. Worse	2. About the same	3. Better
(If you have circled 1 or 3 now please tell us how big the change is)		

If you feel worse,how much worse?

1i   Almost the same, hardly any worse at all

1ii   A little worse

1iii   Somewhat worse

1iv   Moderately worse

1v   A good deal worse

1vi   A great deal worse

1vii   A very great deal worse

If you feel better, how much better?

3i   Almost the same, hardly any better at all

3ii   A little better

3iii   Somewhat better

3iv   Moderately better

3v   A good deal better

3vi   A great deal better

3vii   A very great deal better

Appendix 3

Telephone call proforma

Used at monthly intervals post treatment six times, then at 3-month intervals until 15 months post treatment.

Telephone call script for rehabilitation follow-up

Date of call……………………………………

Introduce yourself on the first call:

My name is xxxxxx xxxxxxxxx and I'm working on the rehab research project. I do the same job as xxxx xxxxxx at the NGH/RHH

I'm ringing you to see how you are at the moment, and to find out how much exercise you are able to do at the present time.

How is your chest today, compared to how it usually is?	Same, better or worse than usual (please circle answer)

If worse than usual please continue with this side of sheet. If same or better, please continue on reverse of sheet.

Worse		
Have you had to change your chest medication or use your inhalers more?	Yes/no	
If yes, what are the changes?		
Have you had to contact the GPs surgery?	Yes/no	
Have you got any new symptoms?	Yes/no	
Can you tell me what the new symptoms are?		If chest pain mentioned, recommend visiting GP. If other symptoms, i.e. leg pain, breathlessness, suggest might like to call physios
Are you still doing the booklet exercises?	Yes/no	If yes, congratulate the patient
Are you doing any other exercise or activity?	Yes/no	If yes, congratulate the patient
If yes to either, how much are you able to do?		
If no to either, have you stopped just because of your current chest problem and intend to restart?	Yes/no	

Signing off

When you started the rehab you were doing half a minute at each station. How about trying to do your booklet exercises for that time again, and next time I ring I hope that you will be feeling better.

Have you still got a telephone number for (name of physiotherapy team members)?

It has been nice talking with you. I will ring again to see how you are getting on. Are there any days that I should avoid?

Same or better		
Are you still doing the booklet exercises?	Yes/no	If yes, congratulate the patient
If no, is there any special reason why not?		Record reason if given
Have you increased your exercise time	Yes/no	If yes congratulate the patient
If yes, how much are you doing now?	30 seconds, 45 seconds, 1 minute, 1 minute 15, 1 minute 30, 1 minute 45, 2 minutes, 2 minutes 15, 2 minutes 30, 2 minutes 45, 3 minutes, 3 minutes 15, 3 minutes 30, 3 minutes 45, 4 minutes, 4 minutes 15, 4 minutes 30, 4 minutes 45, 5 minutes	That's very good
Are you doing any other exercise or activity	Yes/no	If yes congratulate the patient
What additional activity are you doing		
Are you doing any new activities since our last phone call		

Have you still got a telephone number for (name of physiotherapy team members)?

It has been nice talking with you. I will ring again to see how you are getting on. Are there any days that I should avoid?

Appendix 4
Poster presentations at COPD 5

These report work associated with, but not funded by, this study.

They comprise:

(i) Qualitative aspects of the study.
(ii) Minimum clinically significant difference in the ESWT.

Sheffield Teaching Hospitals **NHS**
NHS Foundation Trust

Sheffield Hallam University

HTA
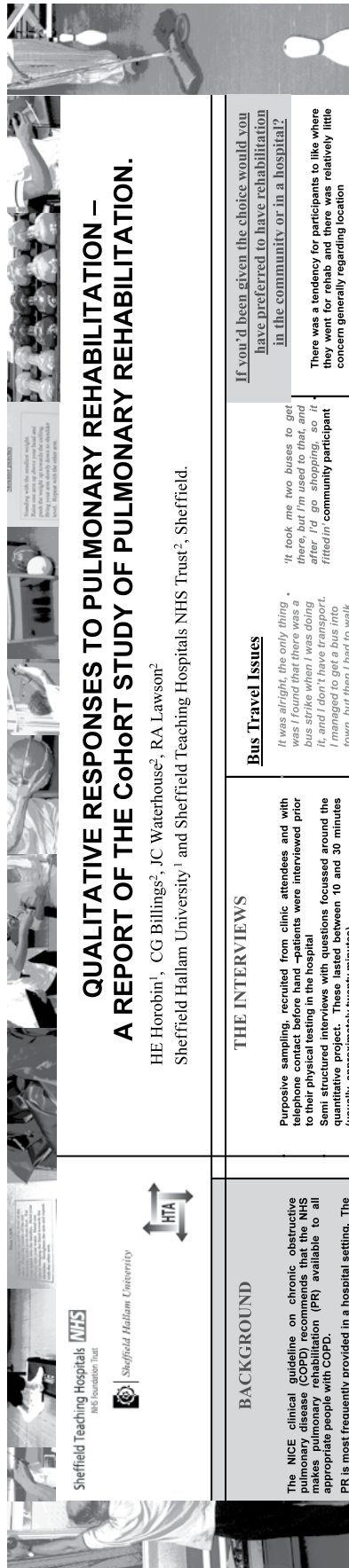
QUALITATIVE RESPONSES TO PULMONARY REHABILITATION – A REPORT OF THE CoHoRt STUDY OF PULMONARY REHABILITATION.

HE Horobin[1], CG Billings[2], JC Waterhouse[2], RA Lawson[2]
Sheffield Hallam University[1] and Sheffield Teaching Hospitals NHS Trust[2], Sheffield.

BACKGROUND

The NICE clinical guideline on chronic obstructive pulmonary disease (COPD) recommends that the NHS makes pulmonary rehabilitation (PR) available to all appropriate people with COPD.

PR is most frequently provided in a hospital setting. The facilities are thus limited and potentially inaccessible and not patient friendly.

- PR performed in a community setting could be preferable in terms of access, and people might "buy in" to lifestyle changes more easily if these were instigated in the sort of place that you do something for yourself rather than a place where you go to have something done "to you"
- The study was funded by the National Coordinating Centre for Health Technology Assessment. The HTA however did not wish to fund any qualitative investigation of preferences and experience. We had been given ethical approval for this arm of the study and believed that the qualitative aspect would give valuable insight so funded a small study together with Sheffield Hallam University

OBJECTIVE

- In addition to the quantitative measures required by the study, we conducted qualitative interviews for a patient perspective on pulmonary rehabilitation and the follow up support with the aim of adding meaning to the quantitative data

METHODS

There were five interrelated stages following ethics processes:
1. initial review of the research and preparation of the structured interviews
2. 2004 summer interviews recorded and transcribed
3. analysis of data with further development of structured interviews
4. 2005 summer interviews recorded and transcribed
5. further data analysis

PARTICIPANTS

17 full course attendees interviewed at 6 months
10 full course attendees interviewed at 12 months
5 full course attendees interviewed at 18 months
– all of these had been interviewed at 6 months
10 poor rehab attendees

THE INTERVIEWS

Purposive sampling, recruited from clinic attendees and with telephone contact before hand –patients were interviewed prior to their physical testing in the hospital
Semi structured interviews with questions focussed around the quantitative project. These lasted between 10 and 30 minutes (usually approximately twenty minutes)
A quiet room was used and the conversation taped with simultaneous note taking
All participants were guaranteed confidentiality and anonymity.
Only 1 research participant refused to be interviewed

THEMATIC ANALYSIS

Transcribed information was read, coded and themes generated
One issue with this type of research is that the questions were formed according to the issues generated by the quantitative study, however participants were free to interpret these questions and also given opportunities to discuss the other issues that concerned them

What did you think about the location of the pulmonary rehab?

- Most came by car or car or taxi, approx a third by bus and a couple by hospital transport (hospital cars)
- Responses from drivers were dominated by parking and access issues, hospitals came in for particular criticism with patients sometimes spending a long time finding a parking space – parking at community locations was easier
- Public transport travelling tended to be more energy demanding for participants
- Community locations increased the time and money cost of travel, both through and increase in the number of buses taken and the non availability of 'hospital' transport
- Difficulties in transport were suggested as a cause of non attendance
- Other location issues included: personal construct ideas, knowing where they were ,where they were going and how much energy this would take, safety, credibility and cost.

Car Access Issues

'there was no problem parking because there was a little car park at the back you see' community participant

'it took me thirty minutes to an hour to park, I was just about to get the phone out and say that I wasn't coming, when someone pulled out and left a space across the road' hospital participant

'The hall location was good, as I could park close to home, it was a nice place and I preferred not being in a hospital, it made it more sort of relaxed' community participant

'I hated trying to find somewhere to park at the hospital, I'd have preferred somewhere nearer to home' hospital participant

Bus Travel Issues

It was alright, the only thing was I found that there was a bus strike when I was doing it, and I don't have transport. I managed to get a bus into town, but then I had to walk to Endcliffe a couple of times. A couple of the chaps gave me a lift back into town a couple of times' community participant *(town to Endcliffe is approx 2 miles)*

'I couldn't afford the bus fare,...' community rehabilitation refuser

'It took me two buses to get there, but I'm used to that, and after I'd go shopping ...so it fitted in' community participant

'a place somewhere outside would have been much harder to get to' hospital participant

'I only lived 10 minutes away, so I walked to rehab and caught the bus back up the hill, getting to rehab anywhere's not really a problem for me' hospital participant

Personal Energy Considerations

'I was worried about parking, I worried about getting there most, rather than doing the thing itself' hospital participant

'Every time you get here, you're knackered, so that's a problem' hospital participant (after walking from the car park)

'in an area that everybody knows is good, because you don't know at a church hall, parking might be even worse' community participant

Safety – Credibility – Cost

'You don't get the same environment, you sit up and listen to somebody in a white coat whereas in the community you might not take so much notice....I would probably walk into a church hall or something and think, well, this isn't exactly a medical centre' hospital participant

'coming to the hospital suited me well, I felt safe in the hospital' hospital participant

'It's cheaper to get to hospital, because if you're going to get hospital transport, it's free' hospital participant

'I had to pay for my own transport, a taxi, for the 2 sessions a week, it made it quite expensive' community participant

How did you find the follow up calls?

Many seemed to have forgotten that they had been called
Of those that did remember, responses were generally positive as it was a demonstration of the hospitals continuing care
Calls were not considered to have had an impact on them

- *'I've forgotten that – I think there was something...'*
- *'nobody cares when you get to 70'*
- *'it was nice, they encouraged me with my exercises'*

If you'd been given the choice would you have preferred to have rehabilitation in the community or in a hospital?

There was a tendency for participants to like where they went for rehab and there was relatively little concern generally regarding location
If a preference was expressed, it was for hospital – for a variety of reasons (familiar, safe, easy re public transport, not sure why)

'I was dreading having to go to a church hall' hospital participant

'I think choice is a personal thing. It would be better in a hospital because that is where the medication is' hospital participant

'I don't mind where I go, assuming that they'd got all the equipment' community participant

'I preferred the hospital, the alternative was Handsworth and that's a long way, but also, one of the ladies on the course was taken quite badly and she was able to be seen straight away which was good' hospital participant

'I don't know why but I feel it's better coming to a hospital, but it was probably just as good in the church hall' hospital participant

What do you think you got out of rehabilitation?

Overwhelmingly what participants feel they achieve from pulmonary rehabilitation is a sense of control of their breathing, this tends to increase self reported confidence and reduced anxiety

'I really enj oyed rehab, it changed my attitude, I realised I wasn't alone. I had more energy and I'm still continuing with the exercises at home, I feel less short of breath now'

'..learning to control by breathing, learning to pace myself..'

'I benefited from the talks, it made me feel more motivated and I cope with my breathing better....it gave me a different outlook'

SUMMARY

The location of pulmonary rehabilitation is a complex and personally constructed issue and dealing with car transport alone will not address the problem for all – particularly non attendees.

Participants in this project tended to prefer hospital based rehabilitation for a variety of reasons.
Telephone follow up calls don't make any self reported difference to adherence.
This research demonstrates that pulmonary rehabilitation results in a better sense of breathlessness control in participants. Participants are perhaps less aware of physical responses, or perhaps this 'breathing control' is how physical improvements are perceived (Nicholls 2003)

Nichols DA (2003) *The Experience of Chronic Breathlessness* Physiotherapy Theory and Practice 19:123-136

PERCEIVED HEALTH BENEFIT AFTER PULMONARY REHABILITATION
A REPORT OF THE CoHoRT STUDY OF PULMONARY REHABILITATION.

JC Waterhouse[1] MC Clarke[1] SJ Walters[2] RA Lawson[1]

Sheffield Teaching Hospitals NHS Trust[1] and School of Health and Related Research, University of Sheffield[2]

BACKGROUND

The NICE clinical guideline on chronic obstructive pulmonary disease (COPD) recommends that the NHS makes pulmonary rehabilitation (PR) available to all appropriate people with COPD.

We are performing a study comparing effect of setting on the outcomes of PR. The primary outcome measure is change in Endurance Shuttle Walking Test (ESWT). This test is performed on the same 10 metre flat walking circuit as the Incremental Shuttle Walking Test (ISWT), but asks the subject to walk at a steady pace at approximately 85% of their estimated VO₂ max. This allows a comparison walk to be carried out at exactly the same walking speed, not forcing the subject to walk faster, it has a greater potential to reflect change in the endurance aspects of PR

Secondary outcome measures involve Health Related Quality of Life (HRQoL). Instruments used include Generic and Disease Specific Questionnaires.

The study was funded by the National Coordinating Centre for Health Technology Assessment

OBJECTIVE

- In a recent UK Health Technology Assessment Board funded study to assess the outcome of pulmonary rehabilitation, per cent change in Endurance Shuttle Walking Test (ESWT) was used as primary outcome measure. Whilst this is a robust, validated measure of exercise capacity, its relationship to perceived change in health is less clear.

- At each assessment visit post rehabilitation the subjects were asked to rate their health change since the last visit. All the HRQoL measurements including this one were completed BEFORE the patient had their endurance shuttle walking test measured.

THE QUESTIONNAIRE

➤ This questionnaire was administered after the subject had completed their other HRQoL questionnaires This was to benefit from them having been thinking of all the effects and was created to collect a "global" impression of HRQoL.

GLOBAL HEALTH CHANGE QUESTIONNAIRE

Since the last time you saw us, has there been any change in your overall health related quality of life?

Has your overall health related quality of life been;

Worse, about the same, better

Subjects answering worse or better were then invited to quantify the magnitude of change, with a choice of:

Almost the same, hardly any better (worse) at all
A little better (worse)
Somewhat better (worse)
Moderately better (worse)
A good deal better (worse)
A great deal better (worse)
A very great deal better (worse)

Description	n	Mean change in time (minutes)	% change in time
WORSE	16	0.15	21
SAME	46	4.39	78
Almost the same, hardly any better at all	0		
A little better	18	3.60	61
Somewhat better	12	5.20	100
Moderately better	27	4.90	92
A good deal better	30	5.98	110
A great deal better	9	6.24	114
A very great deal better	1		

- When self perceived change was classified into three levels (worse, same, better) there was significant evidence (p=0.07) of a difference in change in time walked in the expected direction (people feeling "better" having the greatest increase in walking time)

COMPARISON WITH OTHER HRQoL

Secondary endpoints in the study used HRQoL questionnaires (the generic SF36 version 2 and the disease specific Chronic Respiratory Questionnaire). Comparing the three groups (same, better worse) with these well validated instruments gave similar results
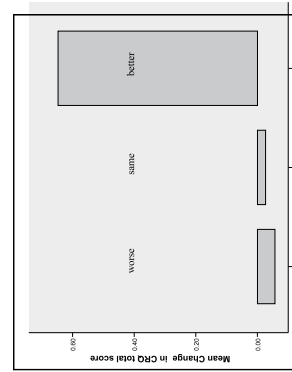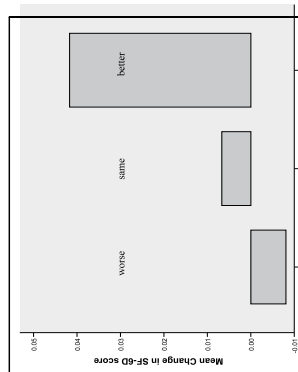
DISCUSSION

A significant group of patients have a large increase in ESWT but express no perceived benefit to their overall health. Physiologists performing the post rehab assessments had anecdotally noted that some people seemed very surprised that the increase in ESWT was so great. Other people were expecting to perform well and were looking forward to finding out just how much better they were.

It is interesting to speculate why this might be.

We suggest that those people who change their lives and are already doing more exercise have realised that they can do more and thus feel that their HRQoL has changed for the better. Those people who have done the PR sessions as a treatment but not extended the things that they do in real life are not aware of the benefits that they have gained from PR.

CONCLUSIONS

An increase in ESWT below 60% is unlikely to result in perceived benefit.

An increase of greater than 100% is required to be confident of benefit.

A significant number of people have objective but not subjective benefits from pulmonary rehabilitation

The global health change questionnaire is a robust instrument

For additional information please contact:

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Appendix 5
Protocol

Comprises final application, response from commissioning board, and reply to commissioning board.

01/15/10: A randomised 2 × 2 trial of community versus hospital rehabilitation, followed by telephone or conventional follow-up; impact on quality of life, exercise capacity and use of health-care resources

The change of project since outline proposal submitted

The fundamental design of the project remains as per the original outline proposal. The core remains a 2 × 2 design, with patients randomised to receive rehabilitation in either a hospital or community setting, followed by either telephone or conventional follow-up. The following changes have been made;

- In addition, it is proposed to collect additional qualitative data to help clarify the cause of any differences in outcome, together with further patient characteristics to amplify the main outcome data.
- In order to ensure this major study is carried out robustly, we have also planned for additional personnel for trial management and data processing.
- Those playing a major role within the steering and scientific committees are defined as applicants. Others whose skills will be drawn on within an advisory committee are defined separately.

Planned investigation
Introduction

Chronic obstructive pulmonary disease (COPD) has a high prevalence throughout the world, and is on the increase (1). This has been emphasised in Sheffield by the SHAIPS2 survey, which shows a particularly high prevalence of COPD in the city,

where nearly 10% of the population over 45 years of age have symptoms of the disease. SHAIPS2 also demonstrated a tight association of disease incidence with indices of deprivation and heavy use of health-care resources (2). In addition to being an important cause of death, the chronic impairment and disability that can result gives rise to both poor quality of life for the individual, and a major economic burden for society (3). By definition, the pulmonary impairment of COPD represents permanent damage that is largely irreversible. Only smoking cessation and long term oxygen therapy (where appropriate) have been shown to have an effect on survival in COPD. The goal of all other therapies is to limit the effects of the disease and endeavour to enhance the patient's quality of life (3).

Three major societies, the British Thoracic Society, the American Thoracic Society and the European Respiratory Society have produce guidelines on COPD. These differ in classification of disease, and in advice in important areas such as use of glucocorticosteroids and theophyllines (4). However, all are agreed that pulmonary rehabilitation is an efficacious treatment that should be widely available. This view was further endorsed by a consensus conference of the Royal College of Physicians held in 2001, the proceedings of which are currently in press, and a meta-analysis of trials has formally confirmed their efficacy in enhancing exercise capability (5).

During the course of COPD, exercise capacity and quality of life are decreased by a number of factors. Although the disease is defined in terms of a test of respiratory function, the FEV_1 (3), this measure actually correlates quite poorly with both quality of life and exercise capacity (6). Often, there is a loss of muscle mass and evidence of detraining (7). A vicious circle is established in which a breathless patient begins to exercise less, so becomes less fit. Exercise is then harder and thus is curtailed further, perpetuating the cycle of decline.

The aim of pulmonary rehabilitation is to arrest this cycle. A key component of the programme is thus an exercise training programme to enhance cardiovascular and muscular fitness. However,

the cycle of decline will be re-established after the programme has stopped unless it is successful in engendering a fundamental shift in the patient's lifestyle. To encourage such lifestyle changes it has become conventional to add an educational programme. One key aim of this is to enable the patient to gain a good understanding of their condition, and thereby to play a key self-management role. It is expected that the patient will make positive choices particularly to maintain increased exercise levels.

The Sheffield COPD Group has adopted the following definition of pulmonary rehabilitation in order to emphasise this;

> 'Pulmonary rehabilitation' is the process of assisting people with respiratory disease to live their life to their full potential, using individualised exercise training with health and lifestyle education, usually within the context of a group.

That a relatively brief period of pulmonary rehabilitation (6 to 12 weeks) can produce an effect that persists as long as 2 years (8) demonstrates that a change in behaviour is occurring, as the effects of exercise training alone would be expected to have vanished long before. Existing research has tended to focus on direct effects of the exercise programme without examining the wider context in which this exercise takes place. A given exercise could, for instance, be viewed as challenging, frightening, exciting, or impossible, depending on the context in which it is presented, and the willingness to voluntarily repeat the exercise would vary as a consequence. The cost-effectiveness of an intervention will critically depend on the duration of effect, yet this has been little studied. The proposed study intends to examine whether the physical context within which the rehabilitation programme occurs is key in determining future outcome, and whether a simple, low cost continued intervention may prolong the treatment effect. It proposes to examine in detail the cost-effectiveness implications of this.

Research objectives

This research proposal intends to answer the following questions;

- Is pulmonary rehabilitation delivered in a hospital outpatient or a community setting more efficacious in acute and long-term effects on exercise capacity and health-related quality of life?
- Is intermittent telephone follow-up efficacious in prolonging the beneficial effects of pulmonary rehabilitation on exercise capacity and health-related quality of life?
- What is the cost-effectiveness of these interventions in pulmonary rehabilitation services?

Existing research

Generally, effects of pulmonary rehabilitation decline over 1 to 2 years (9). It is reasonable to assume that patients who continue to exercise at the end of a rehabilitation programme will experience sustained benefits. Grosbois *et al.*, who adopted various strategies for continuing exercise after pulmonary rehabilitation, have formally shown this. Only those with a continuing exercise maintenance programme demonstrated continuing benefit at 18 months in this particular study (10), with more vigorous interventions producing greater gains. Nevertheless, the fact that benefit may be detectable 2 years after a relatively brief intervention in some studies suggests patients may modify their behaviour after pulmonary rehabilitation, but factors leading to this change have been little studied. There may be a gender effect, with men being helped more by prolonged exercise programmes than women (11). It has proved difficult to demonstrate the direct effect of education, though this has been studied in terms of quality of life rather than exercise capacity (12).

While there have been examples of randomised trials showing the benefit of pulmonary rehabilitation versus 'standard care' for inpatients, outpatients and at the patient's home, no existing trial randomises patients between different venues. The majority of trials have examined hospital inpatients and outpatients, where resultant benefit is clear, or at the patient's home, where results have sometimes been less favourable (13). Community settings for group rehabilitation have been little studied.

Two of the advisory committee members for the proposed study (Sue Ryan and Jenny Elliot) have run a community-based rehabilitation programme. An audit of nine patients (all the individuals in a single programme) showed not only that their average shuttle walk distance improved by 73% at the end of the programme, but remarkably, that there was an *additional* 34% improvement 12 months later. Improvements in breathlessness were likewise maintained over 12 months. Vivienne

Gill, a postgraduate student of Sheffield Hallam University (supervised by Nigel Mitchell, a further advisory group member), used focus groups and questionnaires to judge subjective patient response to the pulmonary rehabilitation programme. This clearly indicated the importance of mutual support, friendship and amelioration of isolation previously caused by COPD. The dissertation concluded that these benefits may have been facilitated by meeting in a community rather than a hospital setting, and that this led directly to the objective success of the programme. An analogous suggestion has been made for a home-based programme, in which the closer links to the domestic situation were felt to be important (14).

A long-term change in exercise behaviour will depend, in part, on psychosocial factors. Importantly, anxiety and depression scores have been shown to improve after pulmonary rehabilitation (15). A study of the health impact of COPD in a Leeds population also used qualitative techniques to suggest several important impacts on global well-being. In particular, 'Quality of life was seen as mainly depending on family relationships, opportunities afforded locally for neighbourliness and freedom from fear, mobility and independence………' (16). Thus it is possible that a community setting for rehabilitation may be more efficacious than a hospital one by facilitating feelings of community and neighbourliness, and avoiding the perceived impersonality and encouraged dependence of a large hospital. The development of mutual support and feelings of control could be strong motivational factors in changing behaviour. Our study proposes to test whether there is a recognisable difference in outcome at the different venues, and if so to give some indication as to the reasons why. It will also assess the cost-effectiveness implications of this.

A number of studies have recognised the declining effect of pulmonary rehabilitation with time and sought to prolong its effect by using supplementary exercise. These have tended to use methods that are intensive of time, such as a 6 week intensive course followed by home follow-up and 'booster' courses (17), 18 month duration exercise programmes (11), 3 months breathing training and physiotherapy, then 3 months supervised exercise daily, followed by 6 months of weekly supervised exercise (18), or a 6 month programme of supervised walking at home following a 2 week hospital-based programme of walking (19). Those studies including comparison with less intensive interventions showed some

outcome benefit from the greater intervention. However, none performed any cost-effectiveness analysis. That a 6 week pulmonary rehabilitation programme is capable of producing a beneficial net cost-effectiveness has been shown (20). It seems unlikely that expensive interventions will produce sufficient increment in benefit to be favourable overall. However, a cheap intervention may do so. The key to prolonged benefit is changed patient behaviour. As reviewed earlier, support, friendship and amelioration of isolation are likely to be key factors. These are easily addressed by telephone follow-up, when encouragement and advice can be given. We propose to test whether telephone follow-up prolongs duration of effect of pulmonary rehabilitation, and whether this is a cost-effective strategy.

Research methods
Recruitment
A current research study under way at the Royal Hallamshire Hospital (RHH) is recruiting subjects seen during routine medical practice at the hospital to a pulmonary rehabilitation research project. No external advertising to patients or to general practitioners has been carried out, but the research project is successfully recruiting numbers equal to those envisaged for the hospital limb of the proposed study. The Northern General Hospital (NGH) sees greater numbers of patients with COPD and would be expected to be able to recruit at least an equal number in the same fashion.

The Sheffield HAZ has been responsible for training health-care workers in COPD and more than half general practices now have a nominated lead individual for COPD. Further practice leads are being identified. Recruitment to the proposed project would occur by advertisement to this lead and subsequent referral for rehabilitation, and by advertisements placed in hospitals, primary care settings and the local press. This would be expected to comfortably yield the additional subjects required in excess of direct hospital referrals.

Prior to the study, patients referred for pulmonary rehabilitation will be reviewed by a respiratory physician (Dr Rod Lawson at RHH, Dr Paul Anderson at NGH) unless already reviewed by a respiratory physician within 4 months. This will mirror the pattern of referral likely to be seen outside a trial setting, enabling the results to be generalised confidently. They will confirm the diagnosis and ensure pharmacological treatment is optimal prior to rehabilitation. Spirometry and reversibility, and oxygenation will be assessed, and

a physiotherapist will perform a clinical assessment to confirm suitability for rehabilitation. Informed consent will be obtained for enrolment into the study, as detailed below.

Patient data

At a baseline visit and at each subsequent assessment visit (immediately post rehabilitation, and 3, 6, 12 and 18 months post rehabilitation), the following assessments will be made (with an additional practice shuttle walk at baseline):

- Shuttle walk distance
- Health-related quality of life measures (CRQ, SF-36, EQ-5D)
- Primary care resource use questionnaire
- Drug use (patients will bring medication for recording)
- BMI, arm circumference and skinfold thickness (used to assess mid arm muscle circumference)
- Questionnaire on use of social services and time off work

These data will be gathered by a researcher not directly delivering the rehabilitation programme itself.

At each telephone follow-up, results of key questions will also be recorded during the structured interview.

Qualitative data

Qualitative data will be obtained from a random selection of 32 subjects, stratified equally between intervention groups. On the basis of previous work (Stevens), and the predicted volume of data capture, it is estimated that response saturation will be achieved with this number of patients.

Subjects will be interviewed at baseline, immediately post rehabilitation, and at 18 months.

The study will employ a qualitative approach using semi-structured interviews to explore and compare respondents' perceptions and experiences of rehabilitation in the two settings. Interviews will be carried out by senior researchers who are used to liaising with clinicians, have experience of conducting qualitative research in sensitive areas and are used to dealing with patients who are severely symptomatic. With the permission of the participant, the interviews will be tape recorded and subsequently transcribed by a professional agency. Tapes will be stored in a locked room, accessible only to researchers working on this project, at the Royal Hallamshire Hospital,

Sheffield until analysed. Researchers not directly connected with patient care will handle all the data. If respondents wish, they will be able to inspect the transcript of their own interview. To verify interpretation, transcripts will be read independently by an experienced researcher who is not part of the project team.

Cost data

Exercise programme

The purpose is to estimate the cost of the programme for each person in each arm of the trial. This is achieved by multiplying the number of sessions attended by each person by an estimate of the average cost per attendee per session. The costs of running an exercise programme include recruitment, administration, hire of facilities, payments to the exercise leaders and the nurses engaged in monitoring. The staff time will be recorded and costed using NHS rates, along with local rentals for facilities, office costs and other directly incurred costs from running the programme. Care will be taken to exclude costs related to the research component of the programme.

Cost consequences

It is anticipated that the expected health improvements achieved through regular exercise would impact significantly on the use of health service resources by reducing the need for secondary and primary care interventions. The use of resources will be recorded over the 18 months of the follow-up. Use of hospital services in terms of inpatient admission (including the length of stay and speciality), outpatient attendances and A&E visits will be obtained from the Sheffield Health Information Project (a well validated linked database of all health services use in Sheffield). The use of primary care will be obtained from self-completed resource use items included in the health follow-up questionnaires. Questions will be asked about recent use of primary care services and be extrapolated to the full 18 months. Use of more expensive drugs will be estimated from patient reports and by asking subjects to bring their chronic drugs to their assessment sessions. Resource use will be costed using national average costs (21). To enable a broader based costing, patients will also be asked about their use of social services and time off work.

Planned interventions

Patients suffering from COPD deemed suitable for pulmonary rehabilitation will be recruited. The two acute hospitals in Sheffield, the Northern General

Hospital and the Royal Hallamshire Hospital, will be paired with the North and West Primary Care Trust (PCT), and the South Eastern and the South Western PCTs, respectively. Each hospital/ paired PCT will have a joint recruitment list for pulmonary rehabilitation. The venue for the rehabilitation programme (community or hospital) will be allocated at random. Patients in the hospital programme will come from either paired PCT, but in community programmes will attend the programme in their local PCT. The community settings will be leisure centres based in the same geographical part of the city. Representatives of Sheffield City Council have agreed to facilitate their use. Leisure centres have been chosen because of their close ties with the local community who use their facilities, and because of the experience of the NHS Beacon Site community cardiac rehabilitation in Newcastle. Here, 40% of its patients continue to attend the general public exercise sessions after completing the rehabilitation course. Continuing to exercise is also a crucial part of maintaining the effects of pulmonary rehabilitation and this setting may promote better compliance with post programme exercise than the hospital setting. Leisure centres can provide the same space and equipment as the hospital settings. The hospitals are each large acute teaching hospitals, both part of the Sheffield Teaching Hospitals NHS Foundation Trust.

Composition of rehabilitation course

Pulmonary rehabilitation will be delivered, whenever possible, by the same individuals in paired hospital and community settings, to minimise variabilities. Data assessment and collection will be made by individuals who are not involved with the primary interventions.

Each course will be preceded and followed by assessment visits as detailed above. One community rehabilitation course will commence each time a hospital rehabilitation course commences, in either one or the other PCT linked to the hospital. Eleven patients will attend for 6 weeks for two afternoon sessions a week each of 2-hour duration. A carer or relative is encouraged to attend. Each session has two elements, exercise and education.

Exercise

A circuit of 10 exercises each graded into three levels, easy, moderate and hard.

The level of exercise and treadmill walking speed the patient begins the scheme on is determined, by set criteria, from the shuttle walk test result

achieved in the initial assessment. All patients on the first session complete 30 seconds at each station.

Heart rate, oxygen saturation and Borg score are recorded at the end of each station.

At the end of the session the average Borg score is calculated for each patient and their station exercise time adjusted to a set criteria for the next session.

All patients are re-shuttle tested at the end of week 3 to adjust the exercise level, to the set criteria, for the remainder of the scheme.

Education element

Week (session)	Professional	Topic
1(1)	Physiotherapist	Breathing control technique
1(2)	Doctor	What is COPD?
2(3)	Nurse	Medication
2(4)	Physiotherapist	Symptom recognition and sputum clearance
3(5)	Occupational therapist	Activity planning and energy conservation
3(6)	Occupational therapist	Stress reduction and relaxation techniques
4(7)		Open discussion
4(8)	Physiotherapist	Healthy lifestyle advice
5(9)	Dietician	Health eating advice
5(10)	Occupational therapist/ Nurse	Managing anxiety
6(11)	Nurse	Benefits advice
6(12)		Open discussion

Inevitably, there will be some patient dropout during this phase, particularly because of exacerbations of COPD occurring during the rehabilitation phase. These are variable, in particular depending on the season of the year. Experience of previous rehabilitation programmes leads us to expect a drop out rate of around 10%. However, we plan to recruit 20% above the numbers suggested by power calculations to ensure recruitment is sufficiently robust.

Following the pulmonary rehabilitation programme either in community or in hospital settings, patients will be randomised to either routine follow-up (i.e. usual patient contact as determined by their usual health-care professionals) or routine

follow-up plus telephone follow-up. The latter will consist of a structured questionnaire enquiring about exercise participation and general lifestyle. This will be repeated at 1, 2, 3, 4, 5, 6, 9, 12 and 15 months. The initial frequent follow-up is intended to consolidate lifestyle changes.

Planned inclusion/exclusion criteria
Inclusion criteria
- Diagnosis of COPD as defined by British Thoracic Society guidelines (3)
- MRC grade 3 dyspnoea or worse despite optimal medical care
- Clinically stable for 4 weeks prior to commencing programme

Exclusion criteria
- Lack of informed consent
- Unwilling/lack of motivation to make lifestyle changes
- Inability to hear and understand educational talks and exercise instructions (hearing aids and interpreters may be used if appropriate)
- Prognosis under 2 years from any disease
- Long-term oxygen therapy or absolute requirement for oxygen therapy on exercise
- Unstable or uncontrolled cardiac disease
- Musculoskeletal problems precluding exercise training

Ethical arrangements
Risks and benefits for trial participants and society
Patients participating in the study will have the benefit of receiving pulmonary rehabilitation. The level of exercise will be individually adjusted for subjects to a level to which they would be expected to be able to exercise at home. Whilst all exercise carries a theoretical risk of musculoskeletal harm or adverse cardiac events, the risk is greatly exceeded by the potential benefit.

Patients with COPD pose a large burden on society in terms of demands on social services and health-care resources. More efficacious and cost-effective treatment would be to the benefit of society in general. Existing evidence suggests favourable cost-effectiveness analysis for pulmonary rehabilitation (20), but this trial will add to this information, and further inform decisions as to the best use of health-care resources.

Informing potential trial participants of risks and benefits
All subjects will receive a written patient information sheet when recruitment to the trial is offered, detailing the rationale behind pulmonary rehabilitation, the benefits and risks and what will be expected of them. Subjects will have the opportunity to discuss this with a member of the trial team, and will be asked to sign to confirm they have read and understood the form.

Informed consent
All potential recruits will receive information as discussed above. They will be asked whether they wish to participate in the study. Those expressing a wish to participate in the study will be asked to sign to confirm their free and informed consent. This will be witnessed by at least one member of the study team and one other individual.

Retention of data
Data relating to the trial will be held for at least 15 years following trial completion.

The primary care team for each subject will receive written information relating to the subject's enrolment in the study, and detailing their progress during the treatment phase.

Sample size
The primary outcome will be the percentage change relative to baseline, i.e. (8 week follow-up – baseline)/baseline, in distance walked (in metres) during the shuttle test. From a study of 20 COPD patients the mean percentage change in distance walked relative to baseline was 188% (SD 343%).

Assuming similar levels of variability, if a difference in mean percentage change of 100% between the community and hospital groups is considered to be of clinical and practical importance. Then to have an 80% power of detecting this difference in means as statistically significant at the 5% (two-sided) level would require 186 patients per group (372 in total). If 20% of patients are lost to follow-up then we need to recruit and randomise 234 per group (468 in total).

To recruit 468 patients at 44 (11 subjects each on 4 programmes simultaneously, i.e. 2 hospital and 2 community) per cycle, will take approximately 11 cycles. However, some of these will be staggered extending the number cycles to 12/13.

One of the secondary outcomes which will be used in the economic analysis will be the SF-6D preference weighted single-index utility score post rehabilitation. From a study of COPD patients the mean SF-6D score was 0.60 (SD 0.126). Assuming similar levels of variability, if a difference in mean SF-6D scores of 0.05 between the Community and

TABLE 1 *Sample sizes required to detect various differences in % change in distance walked relative to baseline in between the hospital and community groups*

Mean difference in change scores	n per group	Total
200%	48	96
175%	62	124
150%	84	168
125%	120	240
100%	186	372
75%	330	660
50%	740	1480
80% power and 5% two-sided significance.		

Hospital groups is considered to be of clinical and practical importance, then to have an 80% power of detecting this difference in means as statistically significant at the 5% (two-sided) level would require 108 patients per group (216 in total).

The trial will include a factorial design (*Table 3*) with the patients randomised to one of four groups. Therefore 468 patients will be randomly allocated to each of the four intervention groups.

TABLE 2 *Sample sizes required to detect various differences in SF-6D score at follow-up between the hospital and community group*

Mean difference in SF-6D scores	n per group	Total
0.10	28	56
0.05	108	216
0.04	167	334
0.03	297	594
0.02	665	1330
SD = 0.13. 80% power and 5% two-sided significance.		

TABLE 3 *Factorial design*

	Community	Hospital
Telephone follow-up	1 (*n* = 117)	3 (*n* = 117)
No telephone follow-up	2 (*n* = 117)	4 (*n* = 117)
1: Community rehabilitation and telephone follow-up.		
2: Community rehabilitation and no telephone follow-up.		
3: Hospital rehabilitation and telephone follow-up.		
4: Hospital rehabilitation and no telephone follow-up.		

Utilising the factorial design we will be able to assess community versus hospital rehabilitation by comparing the 234 patients in groups 1 and 2 with the 234 patients in groups 3 and 4. The primary outcome for this comparison will be the percentage change relative to baseline, i.e. (8 week follow-up – baseline)/baseline, in distance walked (in metres) during the shuttle test.

Similarly we will be able to assess telephone follow-up versus no telephone follow-up by comparing the 234 patients in groups 1 and 3 with the 234 patients in groups 2 and 4. The primary outcome for this comparison will use the repeated assessments of distance walked during the shuttle test at baseline, 8 weeks, 3, 6, 12 and 18 months.

Statistical analysis
The statistical analyses will be performed on an intention-to-treat basis. All statistical exploratory tests will be two-tailed with $\alpha = 0.05$. Baseline demographic, physical measurements (e.g. shuttle walking test), and health-related quality of life data (SF-36, CRQ and EQ-5D) will be assessed for comparability between the treatment groups.

The primary aim is to compare community versus hospital rehabilitation. Secondary aims are to compare telephone follow-up versus no telephone follow-up utilising the factorial design of the trial.

The percentage change relative to baseline, i.e. (8 week follow-up – baseline)/baseline, in distance walked (in metres) during the shuttle test is the primary efficacy response variable. A two independent samples *t* test will be used to compare mean changes between the groups (hospital and community) in this parameter. A 95% confidence interval (CI) for the mean difference in this parameter between the community and hospital groups will also be calculated. Secondary outcomes such as the change in health-related quality of life (SF-36, CRQ and EQ-5D) between baseline and week 8 will be analysed in a similar way.

For the repeated assessments at pre- and post-rehabilitation assessments, and 3, 6, 12 and 18 months after completion of rehabilitation a summary measure such as the area under the curve (AUC) will be calculated for each patient. Mean AUC between the two groups (hospital and community) will then be compared by a two independent samples *t* test. Again a 95% CI for the mean difference in AUCs between the community and hospital groups will also be calculated. The AUC will also be used to assess telephone follow-

up versus no telephone follow-up in the factorial design.

Proposed outcome measures
Shuttle walk distance

Shuttle walk distance is a robust measure of exercise capacity, shown to be sensitive to exercise change produced by pulmonary rehabilitation in patients with COPD (22). Exercise training is the cornerstone to pulmonary rehabilitation. The shuttle walk test is the most direct measurement of exercise outcome and is least subject to further confounding factors, and will thus be used as a measure of exercise capacity. For this reason, this is selected as primary outcome measure.

Health-related quality of life using CRQ, SF-36 and EQ-5D

CRQ will be administered by interview at baseline to help respondents select the areas for measuring dyspnoea. It will subsequently be self-completed. This validated disease specific quality of life questionnaire (23) has been shown to be responsive to changes seen after pulmonary rehabilitation, and has been found to be more sensitive than the St George's Respiratory Questionnaire (SGRQ) and the Breathing Problems Questionnaire (BPQ) (24).

The SF-36 complements the CRQ. It is less sensitive, but provides measures of non-respiratory as well as respiratory consequences of pulmonary rehabilitation. It generates scores on eight dimensions (physical functioning, mental health, social function, pain, physical and emotional role limitations, vitality and general health), summary measures for physical and mental health and a preference-based index (25). It has been shown to be responsive to changes resulting from pulmonary rehabilitation (26, 27). The one page EQ-5D will also be included to provide an additional preference-based measure.

Body composition

Changes in body mass and composition assessed by BMI, arm circumference and skinfold thickness will be measured (28, 29). Tissue depletion is closely linked to quality of life and exercise capability in COPD, and affects on changes in body mass and composition that with time are likely to be important (30).

Economic analysis
Approach

This economic evaluation aims to help health-care commissioners determine whether providing exercise classes in the community is more cost-effective than providing them in hospital and whether providing formal follow up is cost-effective compared to no formal follow-up. The primary economic analysis has taken an NHS perspective, but data will be collected to allow a societal perspective to be taken in the costing.

The appropriate technique of economic evaluation depends on the outcome of the study in terms of costs and health benefits. The simplest scenario would be for one arm of the trial to dominate the other by being either both cheaper and more effective (in terms of health gain), equivalent in cost and more effective, or cheaper and equally effective. However, more complex scenarios may arise where there are conflicts in terms of the different dimensions of health or between costs and health. In such circumstances, the assessment of cost-effectiveness requires a preference-based single index measure of health gain, and preferably one that can be used to consider how the cost of the gains compare with other interventions purchased by the NHS. This can be done informally, within a cost–consequences framework where the decision-maker is left with task of combining the different benefits and comparing them across programmes (31). The preferred approach in economic evaluation is to attempt some kind of aggregation of the benefits using values obtained from the general public.

The method chosen for doing this is to value the benefit of an intervention in terms of quality adjusted life years (QALYs) and compare the two interventions in terms of cost-effectiveness ratios. Where the more costly intervention is also found to be better in terms of health gain, it is then possible to express it as an incremental cost per QALY, and compare this with other interventions purchased by the NHS. The problems and limitations of this approach are well known, but it provides some guidance to the NHS on the cost-effectiveness. The SF-36 data collected in this study will be converted into health state utility values using a recently estimated preference-based algorithm (25). The area under the curve will be estimated between assessments for each individual in the trial to provide an overall estimate of the QALY difference between the intervention and control arm.

Analysis

The main analysis is an intention to treat comparison of the costs of providing exercise in the community compared to hospital, compared to the gains in SF-36 scores at the individual patient level. The final result will be presented as a ratio of the differences in cost and QALY between the arms of the trial, with a 95% confidence interval estimated by bootstrapping. There will be considerable uncertainty in many of the cost estimates and the underlying estimate of benefit. Furthermore, an important consideration in the long-term cost-effectiveness of these interventions is likely to be the longevity of the benefits and cost consequences, particularly of the formal follow-up sub-arms of the trial. It will be important to conduct extensive sensitivity analyses.

Qualitative data

Qualitative interview data will be analysed based on a grounded theory approach (32). Software packages such as QSR NUD*IST will be employed to facilitate analysis. The 'Framework' approach developed by the National Centre for Social Research will be used to identify recurrent themes (33).

Further analyses

Further subgroup analysis will be used. In particular, the effects of disease severity as assessed by FEV_1 and the effects of gender will be examined. These data will be used to generate hypotheses, as the sample size required for formal evaluation within the study would be excessive.

Independent supervision of trials and management structure

A Data Monitoring and Ethics Committee (DMEC) will be established. It will meet prior to patient recruitment and yearly thereafter. As pulmonary rehabilitation itself is established and known to be safe, its main remit will be to ensure an ethical approach to the large numbers of subjects involve, with correct and safe handling of data. It will consist of three individuals with experience of clinical research from outside Sheffield, and will report to the Trial Steering Committee.

The Trial Steering Committee will be chaired by an independent chair from outside Sheffield, with experience in conduct of clinical trials. There will be two further independent members. Each will have experience in the conduct of clinical trials. At least one will have specific experience in pulmonary rehabilitation. Members of the Scientific Committee (see below) will also participate in the Trial Steering Committee.

We recognise the importance of involving consumers in research (34, 35). We plan to invite two consumers recruited from local support groups within Sheffield to sit on the Project Steering Group. We will offer training to these consumers. This will be in the form of either the IMPACT programme, which is operated from the Education Division/CASP from the NHS Public Health Resource Unit or an internal programme operated by the Academic Palliative Medicine Unit at the Royal Hallamshire Hospital. The travel expenses of consumers will be reimbursed and they will be paid on a sessional basis (£15) which is in line with current recommendations issued by the NHS Consumers in Research NHS Support Unit.

The Trial Steering Committee will meet at least once prior to commencement of patient recruitment, and at least a further five times during the conduct of the trial. It will communicate directly with the DMEC, the study co-ordinator and the Advisory Committee (see below).

The Scientific Committee will be formed by the applicants. They will be responsible for ensuring the trial is run in a scientifically thorough and rigorous fashion. They will finalise trial arrangements prior to commencing subject recruitment, and be responsible for adequate training of staff to ensure consistent and complete data capture and recording will occur. They will be responsible for continued monitoring of the trial's progress and interim report generation. They will be responsible for final data analysis and dissemination of results in the form of peer reviewed papers in scientific journals and presentations to scientific societies. The Scientific Committee will meet as necessary to discharge these responsibilities.

The Advisory Committee will be a group of individuals with relevant practical expertise that is both broad and deep. They have agreed to contribute this knowledge to help ensure the study runs successfully, but do not have direct responsibility for it.

A study co-ordinator will providing a key role liaising between the management and implementation groups.

Appendix 1 shows a plan of the proposed management structure.

Project timetable and milestone

Timetable (months)	Milestones
1–2	Study set-up
	Programme scheduling and resource co-ordination
	Training of research staff
	Data recording and analysis preparation
	Development of database
	Early recruitment to rehabilitation programmes
3–20 (26)	Run the rehabilitation programmes
	Recruitment to programmes and study
	Four rehabilitation programmes: 2 community based, 2 hospital based. Programmes run every 6–8 weeks
5–37 (43)	Follow-up telephone calls and assessments
36–48	Data collection and analysis
	Report writing
	Dissemination
	Study closure

Expertise

Rod Lawson has a background in academic medicine, predominantly in inflammatory biology. His PhD was gained for a thesis entitled, 'Neutrophil kinetics in pneumonia'. Currently he is a full time NHS Respiratory Physician. He is lead clinician for COPD at the Royal Hallamshire Hospital, and is a member of the COPD Joint Planning Group of Sheffield Health Authority. He has played a strong role in the development of the city-wide initiative for developing COPD services within the Health Action Zone, whilst facilitating research into COPD. Existing research under way for which he is principal investigator include projects on the use of medical gasses to relieve dyspnoea and targeted delivery of inhaled therapy. He is also site lead for multi-centre studies of the genetics of COPD and subcutaneous pulmonary vasodilators. He is co-investigator in an investigation of the role of *Chlamydia pneumoniae* in exacerbations of COPD and the use of hyper-polarised helium MRI in COPD. He

will perform medical assessments at the Royal Hallamshire Hospital, and participate in overall trial supervision.

Paul Anderson is an experienced respiratory physician. He is also a member of the Sheffield Joint Planning Group for COPD. He has research experience in a range of respiratory diseases. He will perform medical assessments at the Northern General Hospital and help ensure correct standards of medical supervision are available for all study subjects.

John Brazier is Director of the Sheffield Health Economics Group within Sheffield University, which includes 14 trained health economists. His main research interests have been in the measurement and valuation of health outcomes and economic evaluation. He has led research into the first testing of the SF-36 and developing it for use in economic evaluation. He has assisted in economic evaluations of gallstone lithotripsy, minor surgery in general practice, helicopter emergency medical services, screening for osteoporosis, exercise in the elderly, leg ulcer management and the prescription of clodronate to reduce hip fractures in elderly women. He is also involved in a study of the resource and health effects of housing improvement. He teaches and co-ordinates modules on two MSc courses. He will be lead for health economic evaluations.

Stephen Walters is a lecturer in medical statistics at Sheffield University. He has been involved in the design, analysis and reporting of several randomised controlled trials, which have compared new and existing health technologies. He also has extensive experience of analysing health-related quality of life (HRQoL) measures such as the SF-36.

Judith Waterhouse has extensive expertise in respiratory technical measurements and use of quality of life measurements. She heads the Respiratory Function Unit at the Royal Hallamshire Hospital. She has extensive experience in the conduct of significant clinical trials, having been involved in the MRC oxygen study and having been a member of the scientific and steering committees of the multi-centre ISOLDE trial of inhaled steroids in COPD. She will be responsible for training in physiological measurements and administration of quality of life and other assessment tools, ensuring quality control.

Tony Stevens is lecturer in the Academic Palliative Medicine Unit at Sheffield University. He has

extensive skills in qualitative research techniques, including large scale studies of prisoners and of patients in various health-care settings. These have included work with difficult subjects with behavioural problems, and with subjects from deprived areas and ethnic minority backgrounds. He has transcribed interviews and analysed transcripts both manually using the 'Framework' approach and with the QSR NUD*IST software package. As a qualified librarian he has experience of storing, retrieving and handling large quantities of information, and has an effective working knowledge of copyright and data protection. He will be responsible for the qualitative aspects of research, and will advise on data handling and protection.

Mandy Higenbottam and Sarah Warden are hospital-based physiotherapists with experience in establishing, running and maintaining rehabilitation programmes. Sarah Warden is currently employed as a full time researcher on an existing trial of involving pulmonary rehabilitation. Jenny Elliot and Sue Ryan have together established a successful pulmonary rehabilitation programme, one of a small number successfully running in the United Kingdom. The former is a community physiotherapist. The latter is a practice nurse named Nurse of the Year for her work in pulmonary rehabilitation. Hazel Horobin is a physiotherapist and senior lecturer who has extensive experience of pulmonary rehabilitation programmes, who is now involved in teaching and research. Nigel Mitchell is a dietician and senior lecturer who also has an interest in qualitative research. He has supervised qualitative audit of rehabilitation programmes. Together, these individuals will form an advisory committee to assist and advise on content and conduct of the rehabilitation course and subsequent follow-up.

Justification of support required
Salaries

The rehabilitation programmes and telephone follow-ups require a physiotherapist and nurse team to run two programmes (one hospital and one community) every 6–8 weeks. The programmes have been scheduled to maximise resources, account for holidays and sickness and permit some degree of flexibility. The hospital programmes will be supported by service funding and we have thus requested salaries for 1.0 whole-time equivalent (WTE) additional physiotherapist (Senior 1) and two nurses (Band 8); 0.5 WTE for a period of 41 months and 1.0 WTE for a period of 12 months

when the programmes and follow-ups overlap. This will allow new community programmes to be established for the research and appropriate additional facilities.

To separate the rehabilitation programmes from assessments (HRQoL, shuttle walk, etc.) we require a research nurse (Band 9) for 42 months; 0.5 WTE for the first 6 months, 1.0 WTE for the following 29 months and 0.5 WTE for the final 7 months.

The data collection and analysis for the cost-effectiveness element require the skills of a health economist/statistician (RAII). The work will predominantly take place at the beginning and end of the study, so we have requested 0.4 WTE during the first year and 0.6 WTE during the fourth year.

Although essentially a single site study, the complexity of organisation and detail warrants the skills of an overall study co-ordinator for 0.5 WTE (Band 10) throughout the study. This person in this post will assume day to day responsibility for the running of the trial; they will co-ordinate the study and study personnel, assist with data collection and analysis, co-ordinate the meetings of the study committees (e.g. DMEC), manage the financial aspects of the study and assist with report writing.

Development of the patient database, dietetic advice (part of the rehabilitation programmes) and the qualitative research will be supplied through consultancy.

All other personnel input will be supplied by the applicants and in-house R&D resources.

Please note: There is an additional project cost of £16,150 for 40% overheads associated with the salary of the health economist/analyst who will be employed by the University of Sheffield.

Consumables and equipment

A significant cost of the study is the travel allowance for patients to and from their rehabilitation sessions and for subsequent follow-up assessments. It is anticipated that we will be able to arrange a group collection service wherever possible to reduce costs. For this activity we have requested £9240, and a further £500 has been requested over the 4 years for refreshments for patients during their rehabilitation exercise. The community settings will charge for use of their facilities and we have been quoted £50 per week. A small sum of £800 (£400 for each of the first 2

years) has been requested to replenish medical equipment such as oxygen cylinders during the programmes.

We expect that the DMEC will meet four times and the Steering Group six times over the duration of the study. We have allocated £1800 to cover travel and subsistence costs for these meetings.

The use of questionnaires and supply of educational material will cost in the region of £4600 for the study and the cost of telephone follow-ups has been based on a 10–15 minute telephone call per patient.

The majority of equipment that will be used is already available. The study will however require 11 additional wrist pulse oximeters at a cost of £550 each and 2 skinfold callipers (£157 each). A docking station and software to allow download of data from oximeters has been included.

We have also requested a dedicated computer for the main study databse, with appropriate software.

References

1. Anto JM, Vermeire P, Sunyer J. Chronic obstructive pulmonary disease. Eur Resdatabase 2000; 15:1–22.

2. Coy J, Stannford A. The prevalence of COPD in Sheffield and its impact on morbidity and healthcare utilisation. Thorax 2001:Abstract in press.

3. BTS. BTS guidelines for the management of chronic obstructive pulmonary disease. The COPD Guidelines Group of the Standards of Care Committee of the BTS. Thorax 1997; 52 Suppl 5:S1–28.

4. Ferguson GT. Recommendations for the management of COPD. Chest 2000; 117(2 Suppl):23S–8S.

5. Lacasse Y, Wong E, Guyatt GH, King D, Cook DJ, Goldstein RS. Meta-analysis of respiratory rehabilitation in chronic obstructive disease. Lancet 1996; 348(9035):1115–1119.

6. Fuchs-Climent D, Le Gallais D, Varray A, Desplan J, Cadopi M, Prefaut CG. Factor analysis of quality of life, dyspnea, and physiologic variables in patients with chronic obstructive pulmonary disease before and after rehabilitation. Am J Phys Med Rehabil 2001; 80(2):113–20.

7. Casaburi R. Skeletal muscle function in COPD. Chest 2000; 117(5 Suppl 1):267S–71S.

8. Foglio K, Bianchi L, Bruletti G, Battista L, Pagani M, Ambrosino N. Long-term effectiveness of pulmonary rehabilitation in patients with chronic airway obstruction. Eur Respir J 1999; 13(1):125–32.

9. Cambach W, Wagenaar RC, Koelman TW, van Keimpema AR, Kemper HC. The long-term effects of pulmonary rehabilitation in patients with asthma and chronic obstructive pulmonary disease: a research synthesis. Arch Phys Med Rehabil 1999; 80(1):103–11.

10. Grosbois JM, Lamblin C, Lemaire B, Chekroud H, Dernis JM, Douay B, Fortin F. Long-term benefits of exercise maintenance after outpatient rehabilitation program in patients with chronic obstructive pulmonary disease. J Cardiopulm Rehabil 1999; 19(4):216–25.

11. Foy CG, Rejeski WJ, Berry MJ, Zaccaro D, Woodard CM. Gender moderates the effects of exercise therapy on health-related quality of life among COPD patients. Chest 2001; 119(1):70–6.

12. Gallefoss F, Bakke PS, Rsgaard PK. Quality of life assessment after patient education in a randomized controlled study on asthma and chronic obstructive pulmonary disease. Am J Respir Crit Care Med 1999; 159(3):812–7.

13. Wedzicha JA, Bestall JC, Garrod R, Garnham R, Paul EA, Jones PW. Randomized controlled trial of pulmonary rehabilitation in severe chronic obstructive disease patients, stratified with the MRC dyspnoea scale. Eur Respir J 1998; 12(2):363–369.

14. Hernandez MT, Rubio TM, Ruiz FO, Riera HS, Gil RS, Gomez JC. Results of a home-based training program for patients with COPD. Chest 2000; 118(1):106–14.

15. Withers NJ, Rudkin ST, White RJ. Anxiety and depression in severe chronic obstructive pulmonary disease: the effects of pulmonary rehabilitation. J Cardiopulm Rehabil 1999; 19(6):362–5.

16. Guthrie SJ, Hill KM, Muers ME. Living with severe COPD. A qualitative exploration of the experience of patients in Leeds. Respir Med 2001; 95(3):196–204.

17. Engstrom CP, Persson LO, Larsson S, Sullivan M. Long-term effects of a pulmonary rehabilitation programme in outpatients with chronic obstructive pulmonary disease: a randomized controlled study. Scand J Rehabil Med 1999; 31(4):207–13.

18. Guell R, Casan P, Belda J, Sangenis M, Morante F, Guyatt GH, Sanchis J. Long-term effects of outpatient rehabilitation of COPD: A randomized trial. Chest 2000; 117(4):976–83.

19. Behnke M, Taube C, Kirsten D, Lehnigk B, Jorres RA, Magnussen H. Home-based exercise is capable of preserving hospital-based improvements in severe chronic obstructive pulmonary disease. Respir Med 2000; 94(12):1184–91.

20. Griffiths TL, Burr ML, Campbell IA, Lewis-Jenkins V, Mullins J, Shiels K, et al. Results at 1 year of outpatient multidisciplinary pulmonary rehabilitation: a randomised controlled trial. Lancet 2000; 355(9201):362–8.

21. Netten A, Curtis L. Unit costs of Health and Social Care: University of Kent at Canterbury, 2001.

22. Singh SJ, Morgan MD, Scott S, Walters D, Hardman AE. Development of a shuttle walking test of disability in patients with chronic airways obstruction. Thorax 1992; 47(12):1019–1024.

23. Guyatt GH, Berman LB, Townsend M, Pugsley SO, Chambers LW. A measure of quality of life for trials in chronic lung disease. Thorax 1987; 42(10):773–778.

24. Singh SJ, Sodergren SC, Hyland ME, Williams J, Morgan MD. A comparison of three disease-specific and two generic health-status measures to evaluate the outcome of pulmonary rehabilitation in COPD. Respir Med 2001; 95(1):71–7.

25. Brazier J, Roberts J, Deverill M. The estimation of a prefernce-based single index measure for health from the SF-36. Journal of Health Economics 2001; In press.

26. Benzo R, Flume PA, Turner D, Tempest M. Effect of pulmonary rehabilitation on quality of life in patients with COPD: the use of SF-36 summary scores as outcomes measures. J Cardiopulm Rehabil 2000; 20(4):231–4.

27. Boueri FM, Bucher-Bartelson BL, Glenn KA, Make BJ. Quality of life measured with a generic instrument (Short Form–36) improves following pulmonary rehabilitation in patients with COPD. Chest 2001; 119(1):77–84.

28. Gray GE, Gray LK. Validity of anthropomorhic norms used in the assessment of hospitalised patients. J Parent Nutr 1979; 3:366.

29. Bishop CW, Ritchey SJ. Evaluating upper arm anthropomorphic measurements. J Am Diet Assoc 1984; 84:330–335.

30. Mostert R, Goris A, Weling-Scheepers C, Wouters EF, Schols AM. Tissue depletion and health related quality of life in patients with chronic obstructive pulmonary disease. Respir Med 2000; 94(9):859–67.

31. Drummond MF, O'Brien B, Stoddart GL, Torrance GW. Methods for the economic evaluation of health care programmes. 2nd ed: Oxford Medical Publications, 1997.

32. Glasser BG, Strauss AL. The discovery of grounded theory: Chicago: Aldane Publishing, 1967.

33. Bryman A, Spencer L. Qualitative data for applied policy research. In: Bryman A, Burgess RG, eds. Analysing qualitative data. London: Routledge, 1994.

34. Hanley B, Truesdale A, King A, Elbourne D, Chalmers I. Involving consumers in designing, conducting and interpreting randomisedcontrolled trials: a questionnaire survey. BMJ 2001; 322:519–523.

35. Oliver S, Milne R, Bradburn J, Buchanan P, Kerridge L, Walley T. Involving consumers in a needs-led research programme: a pilot project. Health Expectations 2001; 4(4):18–28.

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Appendix 1 – Proposed management structure
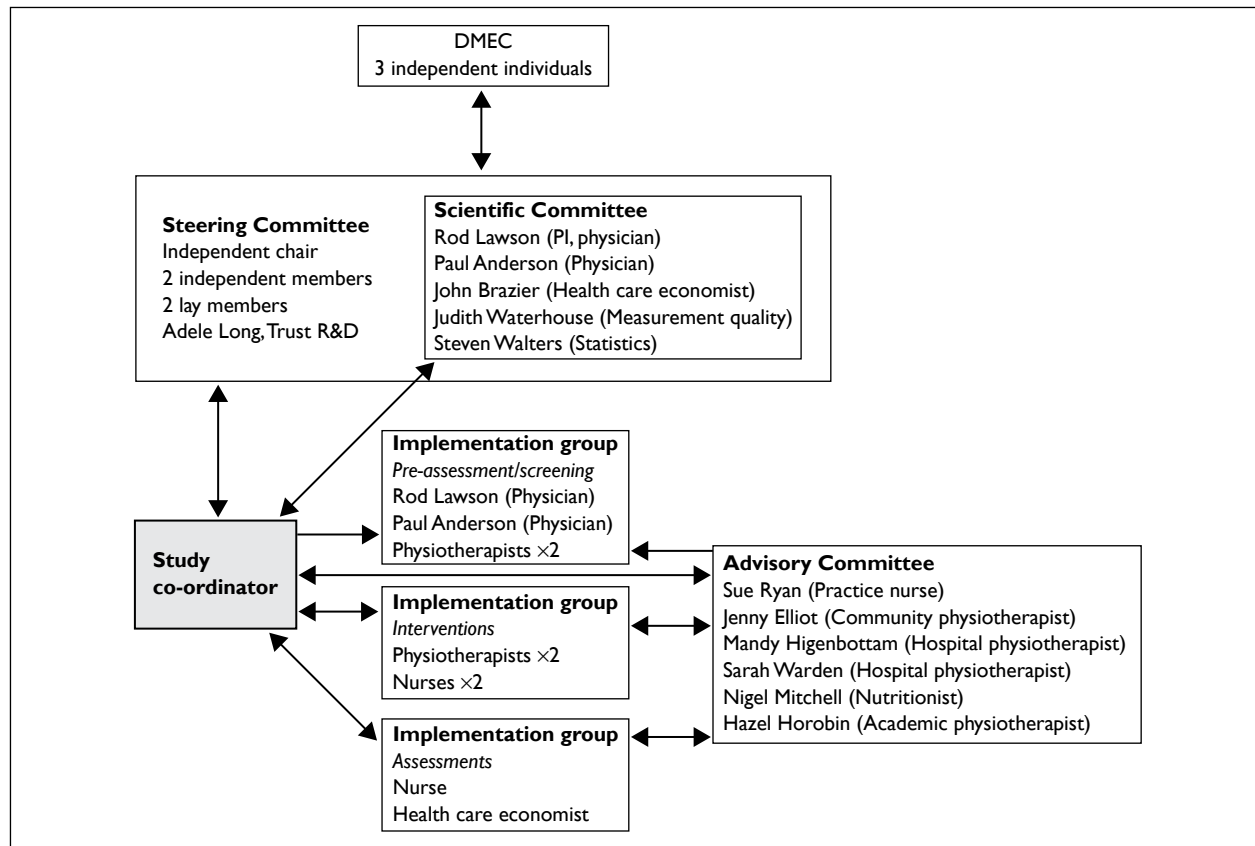
HTA Commissioning Board December 2001

01/15 Pulmonary rehabilitation for chronic obstructive pulmonary disease
01/15/10

1. The proposed qualitative work should be removed from the study, and the costs adjusted accordingly. It is too small an element to be useful.

2. The expertise on the team needs to be increased to include an experienced triallist.

3. The interaction effects between the two intervention arms need consideration.

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