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## ORIGINAL RESEARCH

# The feasibility of recruiting patients with early COPD to a pilot trial assessing the effects of a physical activity intervention

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## Abstract

**Aim:** To determine the feasibility of recruiting patients with early chronic obstructive pulmonary disease (COPD) to the Health Enhancing Activity in Lung THerapy (HEALTH) exercise and education programme.

**Methods:** Patients with early COPD were identified from general practices. Those meeting the study inclusion criteria were administered tiotropium throughout the study period. Participants were randomised to either an eight-week health enhancing and physical activity (HEPA) programme, or to a control group (usual care). Behavioural, physiological and psychosocial outcome measures were reported pre- and post-intervention.

**Results:** Out of 27 practices approached, 16 (59.3%) agreed to participate. Of 215 potentially eligible patients contacted, 60 (27.9%) replied. Twenty (33.3%) were randomised to either HEPA intervention (n=10) or usual care (n=10). Fourteen patients attended a post-intervention assessment.

**Conclusion:** This study provides valuable information on the feasibility of conducting such a trial involving a physical activity intervention.

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**Keywords** exercise, quality of life, physical self-perceptions, COPD, activity, outcomes, pilot study

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## Introduction

The feasibility of conducting randomised controlled trials (RCTs) in primary care requires extensive research to investigate the service implications arising from the introduction of new interventions.[1-3] Feasibility studies may provide valuable information concerning methodological and practical considerations associated with the recruitment of practices and patients for larger clinical trials.

Pulmonary rehabilitation (PR) is recommended as an effective strategy that may be used to alleviate symptoms and optimise the functional capacity of patients with chronic obstructive pulmonary disease (COPD).[4-7] However, a considerable proportion of eligible patients decline participation or drop out of PR programmes.[8,9] Interference with daily routines and being away from home for a period of time, among other reasons, may influence the recruitment and retention of patients.[9] PR is designed for patients with both symptoms and disability from COPD, usually classified on the Medical Research Council (MRC) dyspnoea scale as 3 or higher.[10] However, the benefits and acceptability of PR in

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patients with early disease recruited from primary care is not known. It has been suggested that research needs to focus on the benefits of physical activity in patients with early COPD.[11]

Long-acting bronchodilators are recommended as first-line treatment for patients with any stage of COPD who require maintenance therapy.[12] Inhaled tiotropium is recommended by the National Institute of Clinical Excellence (NICE) for patients whose symptoms are not adequately controlled by short-acting bronchodilators.[10] Tiotropium improves lung function, exercise capacity and dyspnoea, reduces the incidence of exacerbations,[12-17] and in one study enhanced the benefits of an 8-week PR programme in patients with moderate to severe COPD status;[17] the latter study demonstrated larger improvements in lung function, exercise capacity (endurance time), dyspnoea, and health status in patients receiving PR and tiotropium versus PR alone. However, a shorter 6-week PR programme did not provide any additional benefits to patients with COPD already receiving tiotropium.[18] As the outcome of optimal drug therapy and rehabilitation remains unclear, further research is necessary to assess the potential utility of combining PR and tiotropium to treat patients with early COPD.

The purpose of the Health Enhancing Activity in Lung THerapy (HEALTH) study was to determine the feasibility of recruiting patients with early COPD to a pilot RCT. Early COPD was established using the Global Initiative for Chronic Obstructive Lung Disease (GOLD[12]) stage II criteria (forced expiratory volume in one second ($FEV_1$) 50-80% of predicted), equivalent to NICE guidelines for mild COPD. The trial was designed to assess the pragmatic question of the additional effect of an 8-week health enhancing physical activity (HEPA) programme on physiological and psychological outcomes in COPD patients classified as GOLD stage II who were receiving tiotropium in accordance with NICE guidelines.

This paper describes the feasibility of the HEALTH study and critically examines the difficulties encountered with participant recruitment.

## Methods

### Study design

The study was a single-centre, multi-practice, randomised, parallel-group clinical trial. The trial aimed to assess the feasibility of recruiting patients classified as GOLD stage II COPD into an RCT. Patients were diagnosed according to GOLD[12] criteria and were considered to have symptoms inadequately controlled by short acting bronchodilators. Prior to entering the study all patients were either already taking tiotropium or were prescribed tiotropium according to NICE guidelines by their general practitioner (GP) to ensure optimal drug treatment and standardised therapy. Participants were screened for eligibility, and assessed at baseline and immediately post intervention (Figure 1).

Ethical approval was obtained from the Devon and Torbay Local Research Ethics Committee and local Research Management and Governance Units.

### Participants

The study population was established from patients recruited from primary care GP practices in Exeter and the surrounding area. Patients were required to have a clinical diagnosis of GOLD stage II COPD ascertained by a series of inclusion and exclusion criteria (see Table 1). Potentially eligible patients also had symptoms that were considered to be inadequately controlled by short-acting bronchodilators, as determined by their GP. Patients had to be willing and able to undertake a HEPA programme, and were required either to commence or continue treatment with tiotropium in accordance with NICE guidelines.

### Study procedures

#### *Practice recruitment and patient identification*

A total of 27 practices were invited to take part in recruitment. Participating practices performed a search of the patient records in order to identify patients meeting the inclusion and exclusion criteria. Following GP approval, patients were sent an invitation letter on practice headed notepaper with details about the trial. A single reminder letter was sent to non-respondents three weeks after the initial

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**Figure 1. HEALTH study procedure.**

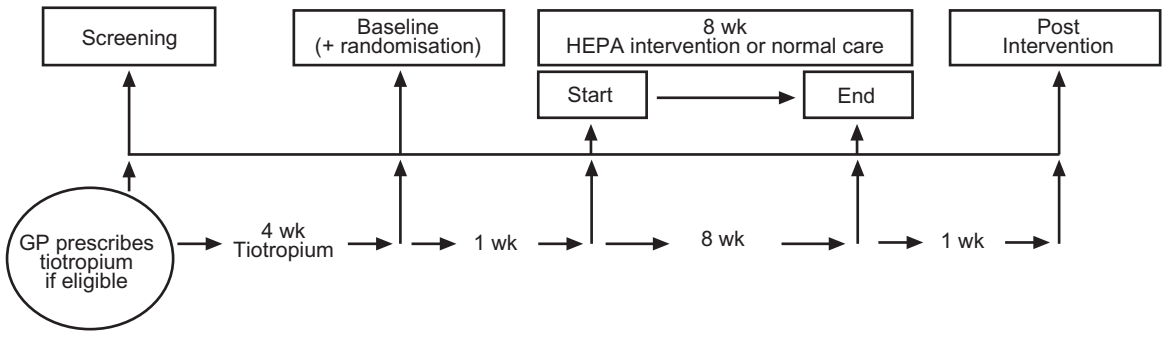




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**Table 1. HEALTH study participant inclusion and exclusion criteria.**

| Inclusion | Exclusion |
|---|---|
| $FEV_1$ between 50% to 80% expected post bronchodilator* | Body mass index (BMI) > 35 kg·m$^2$ or < 18 kg·m$^2$ |
| $FEV_1$/forced vital capacity (FVC) ratio ≤ 70% | History of asthma |
| Bronchodilator reversibility in $FEV_1$ < 15% (4 puffs salbutamol via spacer) | Recent respiratory tract infections |
| Smoking history > 10 pack years | Oxygen desaturation ($SaO_2$) at rest < 90% |
| | Prior participation in a PR programme |
| | Serious co-morbid condition which would interfere with regular exercise training |

* Short-acting bronchodilators included Salbutamol, Ipatropium bromide and Terbutaline

invitation letter. Respondents attended a screening assessment to determine eligibility to participate in the study based upon the inclusion and exclusion criteria (see Figure 1).

Eligible patients were invited to participate in the study and provided informed consent. The research team contacted each patient's GP informing them of their inclusion into (or exclusion from) the study, and for participants not already receiving tiotropium, whether tiotropium would be required to be prescribed. Patients then met their GP who prescribed tiotropium for suitable patients for a minimum of 4 weeks (18 mcg once daily), before attending a baseline assessment.

The randomisation sequence, stratified for smoking status, was computer generated by a statistician who was independent of the trial. Group allocation was kept concealed by means of sealed envelopes which were only opened in sequence by the trial researcher following baseline assessment. It was not possible to blind patients or GPs to group allocation. Given the nature of the intervention it was also difficult to blind researchers from group allocation.

## Outcomes

The following outcomes were assessed at baseline and eight weeks post-randomisation (i.e. post-intervention or after usual care; Figure 1):

- Anthropometric characteristics were assessed including height, weight (SECA, Hamburg, Germany) and BMI.
- Post-bronchodilator spirometry (Koko K298013 Spirometer, Louisville, USA) measured $FEV_1$ expressed as % of predicted, $FEV_1$/forced vital capacity (FVC) ratio, and inspiratory capacity (IC).
- MRC dyspnoea score[19]
- $SaO_2$ using a pulse oximeter (9500 Onyx, Plymouth, USA)
- An incremental shuttle walking test (ISWT)[20]
- A Borg Breathlessness score[21]

In addition, the following questionnaires were completed: the chronic respiratory disease questionnaire (CRQ),[22] lung information needs questionnaire (LINQ),[23] hospital anxiety and depression scale scores (HADS),[24] self-efficacy questionnaire (SEE),[25] seven day physical activity recall questionnaire (7 day PA),[26] physical self-perception profile (PSPP),[27] and smoking status questionnaire.[28]

## HEPA programme and control group

Participants randomised to the HEPA programme attended a once-weekly 90-minute supervised exercise and education sessions delivered by a qualified exercise and health practitioner for a period of eight weeks, within a University exercise facility which is also used by the general public. The HEPA programme included aerobic- and strength- (upper and lower limb) based training exercises, and an educational component undertaken during group discussions to provide participants with a greater sense of understanding and management concerning COPD. The focus group discussions promoted social interaction and provided an opportunity to exchange experiences about COPD management and healthy lifestyles. Each week, group discussion focused on overcoming barriers to, and increasing the perceived benefits of, physical activity. Goals were set for weekly increases in physical activity. Strategies were encouraged to control for symptoms associated with COPD (i.e. breathlessness), and to increase physical activity, social support and perceived competence. To facilitate home-based exercise sessions, participants were provided with an information booklet that included all exercises performed during the supervised HEPA programme. Participants also self-monitored activity levels for motivational purposes throughout the course of the 8-week intervention. Self-monitoring has been shown to increase self-regulatory skills and physical activity and improve health.[29]

The control group received usual care. All participants in both the control and HEPA group continued on tiotropium during the intervention and follow-up period.

## Statistical analyses

As a consequence of the small sample size, it was deemed inappropriate to undertake inferential analysis to compare outcomes in the randomised groups. Using an intention to

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treat approach we present the mean between-group difference (HEPA versus control) and 95% confidence intervals (CI) at follow up for each outcome measure, based on a linear regression model and adjusting for outcome baseline values. All statistical analyses were performed on SPSS version 15.0.

## Results

### Practice recruitment

Of the 27 GP practices in the Exeter area approached for assistance in patient recruitment, 16 (59.3%) agreed to participate. Data obtained from the Quality and Outcome Framework (QOF[30]) 2007/08 revealed that the proportion of COPD patients within 14 of the 16 recruited practices from which data were available was 1.5% – similar to all PCTs in Devon and the UK (1.4% & 1.5%, respectively).

### Patient recruitment

Preliminary record searches identified 806 patients with COPD (435 male; 54%). Of those patients, 383 patients (48%) appeared to meet our inclusion/exclusion criteria after inspection of patient records by the researchers, and were submitted for further vetting by their GP. Of these patients, we were unable to receive confirmation from their GP of suitability for the study for 87 patients and a further 81 were considered unsuitable. The remaining 215 were invited to a screening appointment, of whom 60 (27.9%) replied to our invitation to attend a screening appointment. We did not have ethical approval to send follow-up letters to increase uptake into the study.

Forty-eight patients (22.3% of those invited initially) attended a screening appointment. A further 12 patients responded to the invitation letter but were considered unsuitable for screening. Screening identified 23 of the 48 patients (47.9%) who were eligible for baseline assessment according to the inclusion criteria; of these 23 participants, three withdrew from the study prior to randomisation due to an adverse event (n=2) or competing personal commitments. Thus, 20 patients (all current non-smokers) attended the baseline assessment and were randomised either to the HEPA programme (n=10) or to the control group (n=10) approximately four weeks after screening. Following participant withdrawals post-randomisation – adverse event (n=4); personal commitments (n=2) – 14 participants attended the post-intervention follow-up assessment.

### Post-intervention outcomes

Based on intention to treat for all randomised participants, Table 2 demonstrates the mean difference (95% CI) between groups for each post-intervention outcome measure.

## Discussion

The purpose of the HEALTH study was to assess the feasibility and acceptability of an exercise intervention for patients classified with GOLD stage II COPD. Following the recruitment of 16 practices and the invitation of 215 patients, a total of only 14 patients classified with GOLD stage II COPD completed the post-intervention assessment. This was lower than anticipated, and

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**Figure 2. Patient recruitment to the HEALTH study.**

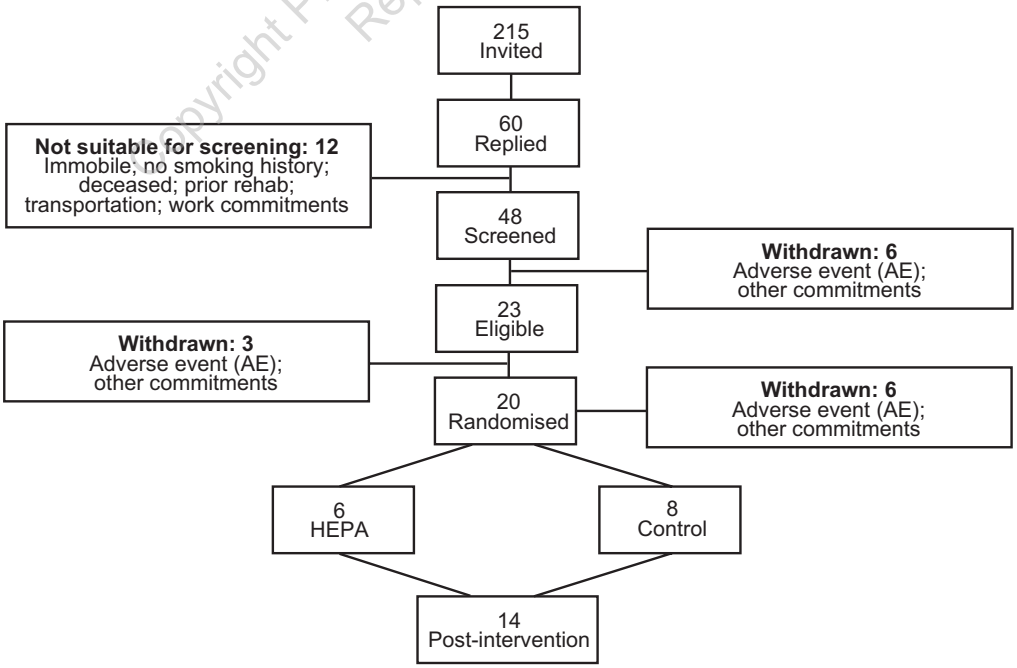




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**Table 2. Mean (± SD) physiological and psychosocial domain scores for control and HEPA participants at the post-intervention follow-up assessment. The mean difference and 95 % CI between the control and HEPA groups are reported for each domain.**

| | Control Mean ± SD | HEPA Mean ± SD | Difference Mean (95% CI)* |
|---|---|---|---|
| $FEV_1$ ($L \cdot min^{-1}$) | 1.69 ± 0.48 | 1.94 ± 0.52 | 0.02 (-0.15 to 0.18) |
| $FEV_1$% predicted | 66.5 ± 12.1 | 65.3 ± 11.9 | 0.6 (-4.7 to 5.9) |
| FVC ($L \cdot min^{-1}$) | 3.11 ± 0.82 | 3.25 ± 0.78 | -0.02 (-0.29 to 0.25) |
| FVC% predicted | 95.4 ± 14.7 | 84.8 ± 14.2 | 2.52 (-4.0 to 9.1) |
| $FEV_1$:FVC ratio | 56.6 ± 9.0 | 60.5 ± 6.7 | 1.7 (-2.3 to 5.6) |
| MRC | 2.5 ± 0.7 | 2.0 ± 0.5 | 0.4 (-0.1 to 0.8) |
| ISWT: Total distance (m) | 362 ± 125 | 399 ± 172 | 12.8 (-74 to 100) |
| ISWT: Borg score | 3.6 ± 1.2 | 3.0 ± 1.8 | 5.1 (-0.7 to 1.7) |
| CRQ: Total | 91.3 ± 20.0 | 90.9 ± 16.4 | -0.4 (-13.8 to 13.0) |
| LINQ: Total | 24.2 ± 10.1 | 21.3 ± 11.5 | 5.9 (-6.8 to 18.7) |
| PSPP: Function | 8.9 ± 1.7 | 9.7 ± 2.5 | -0.4 (-1.9 to 1.1) |
| PSPP: Health | 8.9 ± 1.7 | 8.4 ± 1.0 | 0.1 (-0.9 to 1.1) |
| PSPP: Strength | 8.2 ± 1.8 | 7.4 ± 2.8 | 0.7 (-1.3 to 2.7) |
| PSPP: Self-worth | 9.0 ± 2.6 | 8.2 ± 3.3 | 0.7 (1.0 to 2.5) |
| 7day Total PA (kcal) | 14170 ± 728 | 14311 ± 793 | -85.5 (-807 to 636) |
| HADS: Anxiety | 3.8 ± 3.6 | 3.3 ± 2.1 | 1.0 (-0.6 to 2.7) |

* Adjusted for baseline values

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supports previous research emphasising that difficulties are associated with recruiting patients for clinical trials. This study therefore provides important evidence that may inform future recruitment strategies for trials to assess the benefits of an exercise and education intervention for patients with GOLD stage II COPD. Based on the observed recruitment rate, a multi-centre trial that takes into account the difficulties encountered with the present study is essential to enable a viable future research study. As research has demonstrated the effectiveness of pulmonary rehabilitation in patients with more severe symptoms,[4-7] the present study emphasises the urgent need to undertake large RCTs that will assess the utility of interventions with patients with earlier disease stage characteristics.

A number of recruitment issues were encountered during the study period. The recruitment of GP practices was encouraging, with 59% of invited practices taking part. Of the 11 practices that declined participation, lack of time or interest in research, and having their own pulmonary rehabilitation programmes, were the primary reported reasons. Lack of available time is the most commonly cited reason for GPs to decline partaking in research activities.[3,31] Two participating practices did not wish to consider starting patients on tiotropium for the purposes of the trial and as such only provided access to patients who were already receiving that drug. This supports previous research which suggests that the quality of access to GP practices is equally as important as the quantity of practices recruited.[1]

The recruitment of GPs and patients is a general concern in primary care research and it is widely recognised that recruiting and retaining GPs to participate in research trials in primary care may be challenging.[3,32] In four practices it should be noted that not all patients identified by the study team were vetted by GPs for suitability for invitation to the study. Out of the 138 patients identified from these four practices, 51 were vetted for suitability and mailed, whilst 87 were never checked by their GP for eligibility to be included in the study. This equates to 22.7% of the 'potentially' eligible patients identified by the researchers being undiagnosed. It has been suggested that the pressure of time and forgetfulness of GPs are major factors which may impinge on maximal recruitment.[1] Furthermore, it may be speculated that a centralised University setting for delivering the intervention may have created a barrier for some patients in more outlying recruitment areas.

The extensive inclusion and exclusion criteria, although



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warranted due to the nature of recruiting patients with symptoms characterised as GOLD stage II COPD, may have hindered the study's recruitment success. The recruitment of patients becomes very challenging when interventions are complex or have restrictive entry criteria.[3] GP workload and simplicity of patient eligibility criteria may be primary indicators that influence the effectiveness of recruitment to a research study.[2] Participants were excluded from the study if a single inclusion criteria was not met; accordingly, 52% of patients screened were ineligible to attend the baseline assessment. We feel that this demonstrates not only the impact of the restrictive inclusion criteria on participant recruitment, but also perhaps some of the difficulties associated with recruiting participants from primary care. It may be suggested that a large proportion of the patients excluded at the screening appointment was due to the misdiagnosis of patients with mild to moderate COPD from primary care registers.[33] Research has highlighted that the mislabelling of patients with COPD in primary care may have significant implications for individual treatment and healthcare provision.[34,35] As such, the inclusion of further pertinent information on practice registers may lead to a more accurate diagnosis of patients' disease characteristics.[34] A further 12 patients were also excluded prior to screening due to reasons including immobility, transportation issues, lack of smoking history and work commitments.

Participant retention was affected by the withdrawal of nine eligible patients (39%) due to adverse events (unrelated to the trial) or as a result of commitments (e.g. holidays) prior to, or following, randomisation. Of the 10 participants randomised to the HEPA intervention, six participants regularly attended the weekly exercise and education sessions. The remaining four participants withdrew from the study prior to the first session (adverse event, n=2) or after four weeks of attending the HEPA programme (personal commitments, n=2).

As a result of the limited sample size it was unsurprising that no differences in physical activity (i.e. distance walked in ISWT) or the psychosocial outcome measures at post-intervention assessments were identified between the HEPA and control group participants. Further explanations for this include the following: (1) The exercise and education intervention may have been insufficiently intense and additional formal sessions and goal setting for informal physical activity may be needed;[11] (2) The exercise programme did not exclusively focus on improving the outcomes assessed; (3) Participants in the control group may have increased their physical activity, thereby reducing any differences in outcomes. Nevertheless, the 95% confidence intervals for each of the primary and secondary outcome measures may help to inform prospective future research studies.

Based upon a mean improvement in ISWT seen in several local PR programmes, at an alpha <0.05 (two-tailed), and 87 % power (allowing for 20% participant withdrawal), a sample of 100 participants (50 HEPA programme, 50 control) was desirable. Accordingly, to achieve a sample size of 100 patients based upon the recruitment strategy and inclusion and exclusion criteria reported in the present study (16 GP practices, 20 participants randomised), approximately 80 GP practices with a total COPD register of approx 7000 patients would be required if the approaches taken in this study were used.

## Conclusion

Despite intense efforts, and good practice recruitment, only small numbers of patients with GOLD stage II COPD were recruited to, and successfully followed up, in this study. The conversion rate from identifying suitable patients to randomisation within the study was less than expected. This was probably due to the complex inclusion/exclusion criteria, and challenges faced in recruitment through primary care. Adherence to the intervention for those patients without unplanned interruptions was good, suggesting that a combination of structured, supervised and tailored exercise and motivational strategies for home-based exercise would be appropriate for future studies.

This study provides important evidence that may inform future recruitment strategies into assessing the benefits of an exercise and education intervention for patients with GOLD stage II COPD. Based on these study findings we estimate that to recruit 100 patients it would be necessary to approach approximately 7000 patients on a COPD register. A multi-centre trial would be required to achieve a suitable sample based upon the current inclusion and exclusion criteria. Given the evidence of the effectiveness of PR in patients with more severe COPD, there is now an urgent need to determine whether similar observations apply in the larger group of individuals with earlier disease characteristics.

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### Conflict of interest declarations

In the last 3 years RJ has received speakers fees from Boehringer Ingelheim, Pfizer, GlaxoSmithKline, TEVA, Altana, Astra Zeneca, MSD, Tejin and Trinity Chiesi. RJ has sat on advisory boards related to COPD for Boehringer Ingelheim, Pfizer, GlaxoSmithKline, TEVA, Novartis, and Nutricia in the last 3 years and acted as a consultant to Pfizer and Boehringer Ingelheim. No other author has any conflict of interest.

## References

1. Bell-Syer SEM, & Klaber Moffett JA. Recruiting patients to randomised trials in primary care: principles and case study. *Fam Pract* 2000;**17**(2):187-91. http://dx.doi.org/10.1093/fampra/17.2.187
2. Foy R, Parry J, Duggan A, *et al*. How evidence based are recruitment strategies to randomised controlled trials in primary care? Experience from seven studies.



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*Fam Pract* 2003;**20**(1):83-92. http://dx.doi.org/10.1093/fampra/20.1.83

3. Huibers MJH, Bleijenberg G, Buerskens AJHM, *et al*. An alternative trial design to overcome validity and recuritment problems in primary care research. *Fam Pract* 2004;**21**(2):213-18. http://dx.doi.org/10.1093/fampra/cmh219
4. Nici L, Donner C, Wouters E, *et al*. American Thoracic Society/European Respiratory Society statement on pulmonary rehabilitation. *Am J Respir Crit Care Med* 2006;**173**:1390-413. http://dx.doi.org/10.1164/rccm.200508-1211ST
5. Lacasse Y, Goldstein R, Lasserson TJ, Martin S. Pulmonary rehabilitation for chronic obstructive pulmonary disease. Cochrane Database Syst Rev 2006;4:CD003793.
6. National Collaborating Centre for Chronic Conditions. Chronic Obstructive Pulmonary Disease. National clinical guideline on management of chronic obstructive pulmonary disease in adults in primary and secondary care. *Thorax* 2004;**59**:1-232.
7. American Thoracic Society, European Respiratory Society. ATS/ERS statement on pulmonary rehabilitation: joint ACCP/AACVPR evidence-based guidelines. *J Cardiopulm Rehabil* 1997;**17**:371-405. http://dx.doi.org/10.1097/00008483-199711000-00002
8. Strijbos JH, Postma DS, Van Altena R, Gimeno F, Koeter GH. A comparison between 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**(2):366-72. http://dx.doi.org/10.1378/chest.109.2.366
9. Fischer MJ, Scharloo M, Abbink JJ, *et al*. Participation and drop-out in pulmonary rehabilitation: a qualitative analysis of the patient's perspective. *Clin Rehabil* 2007;**21**(3):212-21. http://dx.doi.org/10.1177/0269215506070783
10. National Institute for Clinical Excellence (NICE). Chronic obstructive pulmonary disease: national clinical guideline for management of chronic obstructive pulmonary disease in adults in primary and secondary care. *Thorax* 2004;**59**(Suppl I).
11. Chavannes N,Vollenberg JJH, van Schayck CP, Wouters EFM. Effects of physical activity in mild to moderate COPD: a systematic review. *Br J Gen Pract* 2002;**52**:574-8.
12. Global Initiative for Chronic Obstructive Lung Disease. Global strategy for the diagnosis, management and prevention of COPD. http://www.goldcopd.org. Accessed August 5, 2008.
13. Casaburi R, Briggs DD, Jr, Donohue JF, Serby CW, Menjoge SS, Witek TJ, Jr. The spirometric efficacy of once-daily dosing with tiotropium in stable COPD: a 13-week multicenter trial. The US Tiotropium Study Group. *Chest* 2000;**118**:1294-302. http://dx.doi.org/10.1378/chest.118.5.1294
14. Littner MR, Ilowite JS, Tashkin DP, *et al*. Long-acting bronchodilation with once-daily dosing of tiotropium (Spiriva) in stable chronic obstructive pulmonary disease. *Am J Resp Crit Care* 2000;**161**:1136-42.
15. Casaburi R, Mahler DA, Jones PW, *et al*. A long-term evaluation of once-daily inhaled tiotropium in chronic obstructive pulmonary disease. *Eur Respir J* 2002;**19**(2):217-24. http://dx.doi.org/10.1183/09031936.02.00269802
16. Brusasco V, Hodder R, Miravitles M, Kirducki L, Towse L, Kesten S. Health outcomes following treatment for six months with once daily tiotropium compared with twice daily salmeterol in patients with COPD. *Thorax* 2003;**58**(5):399-404
17. Casaburi R, Kukafka D, Cooper CB, Witek TJ, Kesten S. Improvement in exercise tolerance with the combination of tiotropium and pulmonary rehabilitation in patients with COPD. *Chest* 2005;**127**:809-17. http://dx.doi.org/10.1378/chest.127.3.809
18. Lindsay M, Lee A, Chan K, *et al*. Does pulmonary rehabilitation give additional benefit over tiotropium therapy in primary care management of chronic obstructive pulmonary disease? Randomised controlled clinical trial in Hong Kong Chinese. *J Clin Pharm Ther* 2005;**30**:567-73. http://dx.doi.org/10.1111/j.1365-2710.2005.00686.x
19. Bestall JC, Paul EA, Garrod R, Garnham R, Jones PW, Wedzicha JA. Usefulness of the Medical Council (MRC) dyspnoea scale as a measure of disability in patients with chronic obstructive pulmonary disease. *Thorax* 1999;**54**:581-6. http://dx.doi.org/10.1136/thx.54.7.581
20. 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**:1019-24. http://dx.doi.org/10.1136/thx.47.12.1019
21. Fierro-Carrion G, Mahler DA, Ward J, Baird JC. Comparison of continuous and discrete measurements of dyspnea during exercise in patients with COPD and normal subjects. *Chest* 2004;**125**:77-84. http://dx.doi.org/10.1378/chest.125.1.77
22. Guyatt GH, Berman LB, Townsend M, Puglsey SO, Chambers LW. A measure of quality of life for clinical trials in chronic lung disease. *Thorax* 1987;**42**:773-8. http://dx.doi.org/10.1136/thx.42.10.773
23. Hyland ME, Jones RCM, Hanney KE. Information needs in COPD patients: the Lung Information Needs Questionnaire. *Airways J* 2005;**3**:142-4.
24. Zigmond AS, Snaith RP. The Hospital Anxiety and Depression Scale. *Acta Psychiatra Scandinavica* 1983;**67**:361-70. http://dx.doi.org/10.1111/j.1600-0447.1983.tb09716.x
25. Perraud S. Development of the Depression Coping Self-Efficacy Scale (DCSES). *Archives of Psychiatric Nursing* 2000;**14**:276-84. http://dx.doi.org/10.1053/apnu.2000.19090
26. Blair SN. How to assess exercise habits and physical fitness. In: Matarazzo JD, Weiss SM, Herd AA, Miller NE, Eds. Behavioural health: A handbook of health enhancement and disease prevention. New York: J. Wiley, 1984, p. 424-447.
27. Fox KR. Advances in the measurement of the physical self. In: Duda M, ed. Advances in sport and exercise psychology measurement. Morgantown, West Virginia: Fitness Information Technology, 1998. p 295-310.
28. Heatherton T, Kozlowski L, Frecker JR, & Fagerstrom K. The Fagerstrom test for nicotine dependence: a revision of the Fagerstrom Tolerence Questionnaire. *Br J of Addiction* 1991;**86**:1119-28. http://dx.doi.org/10.1111/j.1360-0443.1991.tb01879.x
29. Bravata DM, Smith-Spangler C, Sundaram V, *et al*. Using pedometers to increase physical activity and improve health: a systematic review. *JAMA* 2007;**298**:2296-304. http://dx.doi.org/10.1001/jama.298.19.2296
30. http://www.gpcontraact.co.uk (retrieved 3rd February 2009)
31. Dormandy E, Kavalier F, Logan J, Harris H, Ishmael N, Marteau TM. Maximising recruitment and retention of general practices in clinical trials: a case study. *Br J Gen Pract* 2008;**58**:759-66. http://dx.doi.org/10.3399/bjgp08X319666
32. Wilson S, Delaney BC, Roalfe A, *et al*. Randomised controlled trials in primary care: case study. *BMJ* 2000;**321**(7252):24-27. http://dx.doi.org/10.1136/bmj.321.7252.24
33. Jones RC, Dickson-Spillmann M, Mather MJ, Marks D, Shackell BS. Accuracy of diagnostic registers and management of chronic obstructive pulmonary disease: the Devon primary care audit. *Respir Res* 2008;**9**:62. http://dx.doi.org/10.1186/1465-9921-9-62
34. Pearson M, Ayres JG, Sarno M, Massey D, Price D. Diagnosis of airway obstruction in primary care in the UK: the CADRE (COPD and Asthma Diagnostic/management REassessment) programme 1997–2001. *Int J COPD* 2006;**1**:435-43.
35. Tinkelman D, Price D, Nordyke R, Halbert RJ. Misdiagnosis of COPD and Asthma in Primary Care Patients 40 Years of Age and Over. *J Asthma* 2006;**43**:1-6. http://dx.doi.org/10.1080/02770900500448738

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