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Cognitive behavioural therapy combined with physical activity behavioural modification strategies during pulmonary rehabilitation in patients with COPD.

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Take home message: Improvements in daily physical activity (PA) outcomes are optimised when anxious and/or depressed patients with COPD undertake rehabilitation that incorporates a PA behavioural modification intervention alongside cognitive behavioural therapy.

ABSTRACT

Introduction: Patients with COPD who exhibit elevated levels of anxiety and/or depression are typically less able to improve symptoms and physical activity (PA) levels following a programme of pulmonary rehabilitation (PR).

Objective: To provide proof of concept that offering an intervention comprising cognitive behavioural therapy (CBT) alongside PA behavioural modification strategies (BPA) during PR is more effective in improving PA outcomes compared to PR and CBT alone.

<u>Methods</u>: Thirty-two patients with COPD (mean \pm SD: FEV₁: 42 \pm 14% predicted) were assigned 1:1 to receive PR+CBT+BPA or PR+CBT. BPA comprised motivational interviews, step count monitoring, feedback using a pedometer and goal setting. Assessments included accelerometer-derived steps/day, movement intensity, 6MWD and HADS scores.

<u>Results:</u> The magnitude of improvement across PA outcomes was greater for the PR+CBT+BPA compared to the PR+CBT intervention (by 828 steps/day (p=0.029) and by 80 \pm 39 vector magnitude units (p=0.042), respectively). Compared to PR and CBT alone, the PR+CBT+BPA intervention induced greater clinically meaningful improvements in HADS anxiety scores (by -2 units [95% CI -4 to 1 units]) and 6MWD (by 33 \pm 20 m).

<u>Conclusions</u>: Providing anxious and/or depressed patients with COPD with a combined intervention of CBT and BPA during PR, presents more favourable improvements in PA outcome measures compared to CBT alone during PR.

Key words: Cognitive Behavioural Therapy, Pulmonary Rehabilitation, Physical Activity.

Introduction

It is well documented that patients with COPD experience significantly lower levels of physical activity (PA) compared to healthy age-matched individuals (1-4). Alongside this, it is acknowledged that low levels of PA are associated with poor prognosis for exacerbation of COPD, leading to increased rates of hospitalisation and mortality (4). Therefore, interventions to achieve a sustained improvement in PA are urgently needed in this population (2).

Recent systematic reviews and meta-analyses on interventions to promote levels of PA in patients with COPD have, however, reported inconsistent findings (5-7). These interventions included pulmonary rehabilitation (PR), PA counselling as a standalone intervention or alongside PR, health monitoring and nocturnal non-invasive ventilation (NNIV) (5-7). Of these interventions, PA counselling both as a standalone intervention and alongside PR provided the most effective intervention, especially when implemented alongside PR (5, 6). In addition, recent research has shown that although PR is effective for improving functional capacity, it does not necessarily translate into improved PA outcomes unless PA behavioural modification strategies are incorporated (8). Therefore, it is evident that a combination of both PR and behavioural interventions is necessary to see meaningful improvements in PA outcomes.

Interestingly, our earlier systematic review and meta-analysis found that patients with greater baseline PA levels (>4000 steps/day) showed greater improvements in steps/day compared to those with lower baseline PA levels (\leq 4000 steps/day), following a programme of PA counselling (5). In patients with low baseline PA (\leq 4000 steps/day), studies that have implemented PA counselling alongside PR, have reported an insignificant effect on steps/day (9-11). Furthermore, patients with COPD who exhibit lower baseline exercise capacity prior to PR are less likely to achieve significant improvements in PA (12). Indeed, patients demonstrating a 6MWD >350m exhibit clinically meaningful improvements in steps/day compared to patients with a 6WMD \leq 350 m (12). The higher likelihood of PA improvement

in this subgroup of patients is likely because they're more conditioned to cope with the physiological demands of the intervention and have greater self-efficacy, motivation and willingness to engage and improve their PA levels with the support of these interventions (12). In addition, those reporting elevated levels of anxiety and/or depression are typically less able to manage symptoms and less likely to improve PA or 6MWD following PR (13, 14). This may in part be due to anxiety and fear of exacerbating symptoms, leading many to avoid their day-to-day activities as a mechanism to manage their symptoms (15, 16). Meanwhile with depression, people are typically led into a sedentary lifestyle through low mood and poor motivation, which in turn causes further physical inactivity and deconditioning (17).

Cognitive behavioural therapy (CBT) is an evidence-based intervention that can be implemented to help manage symptoms of anxiety and depression in patients with COPD (18). Specifically, Heslop-Marshall et al (18) developed a brief COPD specific CBT intervention that can be delivered by respiratory nurses and demonstrated that two to six fortnightly sessions either in clinic or at home were clinically effective in reducing symptoms of anxiety in patients with moderate to severe COPD. However, in a study implementing CBT alongside PR, similar improvements were shown in depression, anxiety and quality of life symptoms, when compared to PR alone (19). It is therefore envisaged that adding PA behavioural modification strategies to CBT during PR, may optimise improvements in PA outcomes through improved mood and better physical conditioning in this population (13, 14).

In our original study (8), we found that a combination of PA behavioural modification strategies and exercise training during PR was more effective than PR alone in improving PA levels in patients with COPD, characterised by variable levels of anxiety and/or depression. However, the original study did not specifically look at the effects of CBT added to PA behavioural modification strategies during PR on anxious and/or depressed patients with COPD.

Accordingly, in this retrospective analysis of our original study (8), we evaluated the effect of combining CBT with PA behavioural modification strategies (BPA) during PR on PA outcomes (steps/day, movement intensity) specifically in patients with COPD who exhibit elevated anxiety and/or depression levels at the outset of a PR programme. Considering the efficacy of PR+BPA in patients with COPD (8), and the known benefits of CBT to alleviate psychological difficulties in patients with COPD (18), we envisage that a combination of CBT+PR+BPA would be superior to the provision of CBT+PR alone in improving PA outcomes in patients with COPD.

Methods

Study design

This is a retrospective analysis of data from a randomised controlled trial (8) which was prospectively registered at clinicaltrials.gov (NCT03749655) and complied with NIHR HRA requirements (Ref: 18/YH/0376). In this retrospective analysis we focused solely on data from patients with COPD who exhibited high baseline levels of anxiety and/or depression (HADS \geq 8). The cut off (\geq 8) for the diagnosis of anxiety and/or depression using the HADS questionnaire was defined by Nowak et al (20) and was reported to have high sensitivity (80%) and specificity (90%) in patients with COPD (21). This was achieved through the randomisation process in the original randomised controlled trial (8), with 1:1 allocation to either PR +BPA or PR, stratified for HADS (< or \geq 8) and 6WMD (< or \geq 300 meters, Figure 1). Once randomised, those stratified for HADS \geq 8 received CBT as part of standard care provided by the Newcastle upon Tyne Hospitals NHS Foundation Trust (NuTH) on top of their randomised allocation to PR+BPA or PR (i.e.: PR+BPA+CBT or PR+CBT).

Participants

Patients with COPD were recruited from NuTH Chest Clinic and PR services. Respiratory nurses and physiotherapists informed those eligible about the study and asked their willingness

to participate in the study. Inclusion criteria included: (i) COPD confirmed by obstructive spirometry (post-bronchodilator forced expiratory volume in the first second [FEV₁] to forced vital capacity [FVC] ratio <0.70); (ii) clinically stable male or female aged 40 years or older; (iii) optimised medical therapy; (iv) able to provide informed consent. Exclusion criteria included: (i) orthopaedic, neurological or other concomitant disease that significantly impaired normal biomechanical movement patterns, as judged by the investigator; (ii) moderate or severe COPD exacerbation within 4 weeks prior to study enrolment; (iii) unstable ischaemic heart disease, including myocardial infarction within 6 weeks prior to study enrolment; (iv) moderate or severe aortic stenosis or hypertrophic obstructive cardiomyopathy; (v) uncontrolled hypertension or (vi) another condition likely to limit life expectancy to less than one year (principally metastatic malignancy). Upon meeting the study entry criteria, those who agreed to participate were contacted by the research team. Detailed information regarding the study was provided and written informed consent was obtained prior to the study.

Pulmonary Rehabilitation

The 8-week PR programme was delivered according to the BTS guidelines on PR (22), with specific details regarding the PR programme available elsewhere (8). Briefly, the 8-week PR programme was comprised of two 60-minute sessions of exercise training per week, consisting of progressive, individualised aerobic exercise on a cycle ergometer/treadmill and resistance exercises using specific gym equipment/free weights. In addition, a 30-minute session of education was delivered once per week by a multidisciplinary team comprising physiotherapists, dieticians, respiratory nurses, and occupational therapists.

PA behavioural modification intervention (BPA)

Specific details regarding the BPA are available elsewhere (8). Patients received a one-to-one semi-structured motivational interview with the researcher at baseline lasting 15 minutes. During this time, motivational issues, favourite activities, facilitators and barriers to PA and

strategies to become more physically active were discussed (23). Following this, patients created three action plans, which were used throughout the programme to stimulate self-motivation to improve levels of PA.

BPA involved the provision of a pedometer (Fitbug, Camden, London), an individualised daily step-count target (reviewed twice weekly for 8 weeks), and a step-count diary that was shared with a member of the research team at the end of every PR session. Each week, the researcher used the step count diary to calculate a new daily step-count target, by increasing the preceding week's average daily step-count by 10%. In addition, the researcher dedicated 10 minutes following the PR session to provide education on the importance of PA and advice on how to increase PA levels, referring to people's three action plans formed at baseline.

Cognitive Behavioural Therapy (CBT)

CBT lasting approximately 30 minutes was administered to patients with COPD with a HADS ≥ 8 , as part of standard PR service by respiratory nurses at either the Chest Clinic or at home. Specific details regarding delivery of CBT in this study can be found in a previously published RCT (18). Briefly, CBT focused on four key elements: behaviour, cognition/thoughts, feelings/emotions, and physical sensations, with the aim of understanding how these experiences were interpreted (18). Furthermore, to aid symptoms of anxiety and depression, several techniques including education on anxiety, depression and COPD, distraction techniques, breathing control, relaxation and rating achievement/pleasure of PA were used (18).

Outcome measures

All outcome measures were assessed one week prior to the onset of the PR programme and one week following completion of the PR programme. Objective measures of PA, including steps/day, intensity of PA (expressed as Vector Magnitude Units [VMU]) and time spent in various domains of PA (sedentary, light, and moderate vigorous PA) were assessed using the

Actigraph wGT3X (Actigraph LLC, Pensacola, FL, USA), validated for use in COPD (24, 25). Vector magnitude units (VMU), the sum of movements in three planes over each minute, were used to quantify the intensity of daily PA using the Actigraph triaxial accelerometer (Actigraph wGT3X, Actigraph LLC, Pensacola, FL, USA) (26, 27). VMU as an outcome measure is reported as the mean intensity of PA per minute over a specific period of accelerometer wear time, which is outlined below. Patients were instructed to wear an Actigraph accelerometer during waking hours for seven consecutive days, prior to the onset of PR and following completion of PR. Valid PA data from the Actigraph accelerometer were based on a minimum wear time of 8 hours on at least 4 weekdays within the 7-day period (28, 29). Patients experiences of PA were assessed using the C-PPAC instrument, validated for use in COPD (30). The instrument combines 12 questions regarding patients' subjective thoughts on amount and difficulty of PA alongside objective PA outcome data from the Actigraph accelerometer (28). Based on these data, three categories were generated (amount of PA, difficulty of PA and total PA experience) ranging from 0-100, where higher numbers indicated a better score of PA experience. Other outcome measures included: i) the 6MWD (31); ii) quadriceps muscle strength (one leg extension repetition maximum using a calibrated Myometer [MIE Medical Research Ltd, Leeds, UK], and endurance (30 second sit to stand repetitions) and iii) upper body strength (handgrip dynamometer) (32-34); iv) health-related quality of life (QoL) (COPD assessment test [CAT]) (35); v) the clinical COPD questionnaire [CCQ) (36); vi) anxiety and depression (Hospital Anxiety and Depression Scale [HADS]) (37) and vii) MRC dyspnea scale (38).

Data analysis

Characteristics of patients with COPD and outcome data at baseline and following PR are reported as means±SD or 95% confidence intervals (CI) unless otherwise stated. All analyses were completed using SPSS version 28 (IBM corporation, UK), with an intention to treat

statistical analysis used for all outcome measures and missing data handled using a multiple imputation approach. Within and between group differences pre- to post intervention are reported as mean, 95% CI. Independent samples *t* tests were implemented to compare baseline group characteristics. A two-way repeated measures ANOVA was implemented for all outcome variables, to identify differences between the two interventions. Statistical significance was set at p < 0.05 for all analyses.

Results

Participants

In total, 32 patients with HADS \geq 8 (for anxiety and/or depression) provided consent for the study and were randomised to PR+CBT+BPA (n = 17) and PR+CBT (n = 15) (Figure 1). Throughout the study, 8 patients were lost due to: non-respiratory illness (n = 5) and COPD exacerbations (n = 3). Therefore, 24 patients completed the post-PR assessment visit, with 11 completing the PR+CBT+PA and 13 completing the PR+CBT interventions (Table 1). No significant differences in baseline lung function and PA characteristics were reported prior to both interventions (Table 1).

Physical activity outcomes

Individual responses to Actigraph accelerometer-derived PA outcomes are shown in figures 2 and 3. Post PR, the magnitude of improvement in steps/day, was significantly greater (p=0.029) for the PR+CBT+BPA compared to PR+CBT interventions (by 828 steps/day [95% CI 91 to 1564 steps/day], Table 2, Figure 2). This difference was within the clinically important improvement margins (600-1100 steps/day) (39). Following the completion of PR, the PR+CBT+BPA exhibited a significantly greater (p=0.042) improvement in the intensity of PA (by 80 vector magnitude units (VMU) [95% CI 3 to 162 VMU], Table 2, Figure 3) compared to the PR+CBT intervention.

Experiences of physical activity

Individual responses to the C-PPAC instrument are shown in Figure 2. Post PR, the *total score* of the C-PPAC instrument was improved by a clinically important margin (>4 points) (28) in the PR+CBT+BPA intervention compared with the PR+CBT intervention, with a between group difference of 10 points (95% CI 5 to 19 points, p = 0.002, Table 2). For the *difficulty score* of the C-PPAC instrument, a clinically important margin (>6 points) (28) of 13 points (95% CI 5 to 22 points, p = 0.003, Table 2) was found. Finally, the *amount score* of the C-PPAC instrument improved by clinically important margin (>6 points) (28) of 14 points (95% CI 4 to 21 points, p = 0.005, Table 2).

Anxiety and depression

Post-PR, a clinically important difference (<1.5 units) (40), in the magnitude of reduction in HADS Anxiety score (by -2 unit [95% CI -4 to 1 units, p = 0.137, table 3) was demonstrated in favour of the PR+CBT+BPA compared to the PR+CBT intervention. Following completion of PR, a clinically important difference in the magnitude of reduction (<1.5 units) in HADS Depression score was demonstrated across both interventions, with a between group difference of -1 unit [95% CI -3 to 1 units, p = 0.125, Table 3]).

Other outcomes

The 6MWD significantly improved following both PR+CBT+BPA and CBT+PR interventions, with no significant between group differences (Table 3). However, the between group difference $(33\pm20 \text{ m})$ in 6MWD exceeded the clinically meaningful margins (30m, table 3) (41). Both PR+CBT+BPA and CBT+PR demonstrated a clinically meaningful (>2 point) (40) worsening in CAT scores, however the worsening was smaller in the PR+CBT+BPA group (table 3). Significant differences in upper body strength were demonstrated in favour of the PR+CBT+BPA group (Table 3). Significant improvements in lower body strength were

demonstrated in both the PR+CBT+BPA and PR+CBT interventions, however no between group differences in lower body strength were demonstrated (Table 3) **Discussion**

The novel findings of this study suggest that providing anxious and/or depressed patients with COPD with a combined intervention of CBT, PA behavioural modification strategies and PR, presents more favourable improvements in several PA outcome measures including steps/day, movement intensity and experiences of PA, compared to providing CBT alone during PR. The magnitude of improvement in daily PA (by 828 steps/day) in the present study compares favourably with the majority of studies showing clinically important improvements across interventions of PR+PA (9, 10, 42, 43), tele coaching (44) and PA urban training (45) in patients with COPD. Such similarities in PA improvements are fundamental to patients with COPD with elevated anxiety/depression for several reasons. Firstly, previous literature has highlighted the negative impact that anxiety and/or depression may have on baseline levels of PA and the associated link between low levels of PA and increased risk of hospitalisation and mortality (4, 17). This is particularly relevant in the current study, as the average baseline PA levels of our study population (2960 steps/day) were substantially lower than the average levels reported in previous studies implementing PR+PA in patients with COPD (approximately 4200 steps/day) (9, 10, 42, 43, 46). Linking closely to this, it has recently been evidenced that reduced baseline PA levels will likely constrain the effectiveness of PA interventions of this nature, highlighting the importance of our findings (5).

Accordingly, it's important to recognise the justification for these findings and gauge a better understanding of why the combined PR+CBT+BPA intervention may more effectively support physically inactive patients with COPD, compared to the CBT+PR intervention. Considering CBT, which is based upon a model of "talking therapy", patients can focus their negative thoughts and emotions on specific events that cause behavioural avoidance and explore the reasoning behind them (47). Through the phrase "it's not the event, but what individuals make of the event that is important", patients are able to identify unhelpful thoughts and behaviours, relieving anxious and depressive thoughts during stressful events such as exercise (47). Subsequently, patients with COPD are less fearful during daily physical activities, preventing the vicious cycle of panic and avoidance during unexpected stages of breathlessness (16). However, as reported in the CBT+PR group, simply alleviating anxious and/or depressive thoughts and emotions through CBT and improving exercise capacity through PR, does not automatically translate into improved PA levels. One reason for this links to the vicious cycle of inactivity model (48). Within this, two vicious cycles, characterised by dyspnea and/or deconditioning, lead to worsening of anxiety and/or breathing sensations during PA. As a result, patients begin to change their PA behaviour, choosing a sedentary lifestyle over greater levels of PA in response to the symptoms associated with their condition (49). Therefore, the addition of PA behaviour change techniques such as goal setting, action planning and self-monitoring, alongside CBT and PR, may empower and motivate anxious/depressed patients with COPD to engage in more daily physical activities (8, 50).

Based on the novel findings of this study, it is plausible to suggest that through the mechanisms of behavioural modification strategies, PR, and CBT, as detailed above, deconditioned patients with COPD may improve PA by clinically meaningful margins. Furthermore, if these improvements can be replicated across future studies and clinical practice, patients may see additional improvements in key clinical outcomes including exacerbation risk, and hospital admissions, due to their close association with sustained improvements in PA (4, 51-54).

Another relevant finding from this study was the clinically important difference in anxiety following completion of the CBT+PR+BPA intervention, emphasising the potential beneficial effects of combining CBT with PA behavioural strategies on anxiety. One proposed reason for this may link to the previously detailed association between anxiousness and PA in patients

with COPD, particularly with reference to fear avoidance (55). Specifically, a recent study provided preliminary evidence that disease-specific anxiety and fear avoidance have a specific influence on predicted PA levels in patients with COPD who displayed lower relative physical capacity (55). As a result, the smaller improvement in anxiety in those undertaking CBT+PR may have been associated with the poor baseline physical capacity and PA levels, leaving patients in continuous fear and avoidance of PA.

A clinically important difference in 6MWD following completion of both interventions was reported, confirming the effectiveness of PR for improving exercise capacity (56). Interestingly, those who completed the CBT+PR+BPA intervention experienced superior improvements in 6MWD, which exceeded the clinically meaningful margin (30 m). Importantly, a significant improvement for the intensity of PA was found for the CBT+BPA+PR intervention, with a significant between-intervention magnitude of change in intensity of PA. It's plausible to suggest that the reduction in anxiety and fear as well as greater confidence in managing symptoms during daily activities would encourage patients to complete daily activities at a greater pace/intensity (16). In turn, these greater intensities may have translated into improved experiences of PA, as reported through the significant improvement in C-PPAC instrument outcomes. The clinical relevance of this finding is important due to the severe reduction in walking pace typically reported in patients with severe COPD, that is known to be associated with poor prognosis (57). Often, the intensity of PA presents an indication of a patient's ability to conduct PA, providing a breakdown of the time taken to complete a task. Unlike steps/day, which gives an overall accumulation of activity over a set period, the intensity of PA provides better understanding of how patients' symptoms impact PA and how they cope/engage with daily tasks (57). Through observing improvements in both the duration (steps/day) and intensity (VMU) of PA, its plausible to suggest that patients in the current study were able to increase both the amount of walking activity and the pace at which walking activity was undertaken.

Based on the novel findings of this study, it's important to highlight that despite the equally poor PA levels (\leq 4000 steps/day) and 6MWD (\leq 350m) across all patients with COPD in both the PR+CBT+BPA and PR+CBT groups, the combination of PR+CBT+BPA resulted in greater improvements for several outcomes including PA and 6MWD compared to PR+CBT. These findings provide vital evidence that combining the three elements of this intervention can challenge earlier claims that PA counselling interventions alongside PR are effective in improving PA levels only in patients with COPD exhibiting greater levels of PA (>4000 steps/day) and exercise capacity (>350 m) at baseline (9-12).

Study limitations

Several limitations should be considered from this study. Firstly, this retrospective analysis was unable to assess the true effect of CBT. This was due to CBT being part of standard care across NuTH, meaning we couldn't modify standard care for the purpose of this research. Secondly, eight out of 32 patients were lost during the study meaning that only 24 patients with COPD completed both pre and post assessments. As a result, generalisability of the findings to clinical practice may be limited at this stage. Nevertheless, the 25% drop out rate across the study duration is in line with the average dropout rate reported by the UK National COPD Audit Programme for pulmonary rehabilitation (58). Thirdly, CBT engages several techniques including education on anxiety and depression, thereby aiding the mitigation of the intensity of these symptoms. Nevertheless, despite our finding of a clinically important difference in anxiety following completion of the CBT+PR+BPA intervention, we cannot reliably confirm that the additional contact with the CBT specialist did not assist patients to improve their mental health, contributing to the observed benefit. Furthermore, all components of the intervention (CBT, PR & BPA) included factors that are difficult to keep separate while being delivered

collectively (e.g., the PR+CBT group may receive elements of behaviour change which may contribute to BPA). Indeed, exercise training as part of PR may aid improvements in daily PA, albeit to a smaller extent (5). Finally, due to the intervention and all outcome measures being administered by a single researcher in a face-to-face manner, blinding of assessors was not possible. Our inability to blind assessors and those receiving the intervention may have reduced the overall quality of evidence and increased the risk of bias towards the intervention, however due to the study protocol this was unavoidable.

Conclusion

Incorporating CBT and PA behavioural modification interventions into a standard PR programme, may provide patients with COPD who exhibit low baseline levels of PA and elevated anxiety and/or depression with clinically important improvements in PA levels and experiences of PA, alongside improvements in exercise capacity, health-related quality of life and anxiety. Further development and delivery of this combined intervention may support the management/treatment of patients with COPD who exhibit high levels of anxiety and/or depression, consequently lowering the risk of hospital admissions, morbidity, and mortality, associated with physical inactivity in COPD.

Conflict of interest

Dr Matthew Armstrong – I have no conflicts of interest to disclose for this study. Dr Emily Hume – I have no conflicts of interest to disclose for this study. Laura McNeillie – I have no conflicts of interest to disclose for this study. Francesca Chambers – I have no conflicts of interest to disclose for this study. Lynsey Wakenshaw – I have no conflicts of interest to disclose for this study. Dr Graham Burns - Received a grant from NIHR for a CBT study Dr Karen Heslop-Marshall – Received a grant from NIHR for a CBT study and director of pivotal healthcare training for CBT skills. Professor Ioannis Vogiatzis – I have no conflicts of interest to disclose for this study.

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Tables and figures

 Table 1. Baseline characteristics.

PR+CBT+BPA	PR+CBT	P value
(n=17)	(n=15)	
66±4	71±5	0.306
4/13	7/8	n/a
27±7	25±5	0.493
1.07 ± 0.40	0.94 ± 0.50	0.155
2.19±0.60	2.01±0.60	0.676
44±16	41±12	0.098
71±20	73±40	0.445
49±13	46±14	0.228
276±22	259±23	0.161
3972±437	2962±466	0.217
6±2	6±2	0.537
29±1	25±1	0.666
13±1	11±1	0.075
11±2	10±2	0.579
	66 ± 4 $4/13$ 27 ± 7 1.07 ± 0.40 2.19 ± 0.60 44 ± 16 71 ± 20 49 ± 13 276 ± 22 3972 ± 437 6 ± 2 29 ± 1 13 ± 1	66±4 71±5 4/13 7/8 27±7 25±5 1.07±0.40 0.94±0.50 2.19±0.60 2.01±0.60 44±16 41±12 71±20 73±40 49±13 46±14 276±22 259±23 3972±437 2962±466 6±2 6±2 29±1 25±1 13±1 11±1

Values represent mean±SEM for: BMI: Body Mass Index, FEV1: Forced Expiratory Volume in 1 second, FVC: Forced Vital Capacity, 6MWD: Six Minute Walk Distance, PA: Physical activity, MVPA: Moderate Vigorous Physical Activity, CAT: COPD Assessment Test, HADS: Hospital Anxiety and Depression Scale, n: Number

	Group	Baseline	Post PR	Within Group Mean Difference	P values	Between Group Difference	P values
Steps/day	PR+CBT+BPA	2972±437	3920±422	947±247	0.001	828±360	0.029
	PR+CBT	2962±466	3018±450	119±262	0.654		
Intensity of PA (VMU)	PR+CBT+BPA	311±37	362±38	51±27	0.063	80±39	0.042
	PR+CBT	298±39	266±41	-31±28	0.278		
Sedentary time (min/day)	PR+CBT+BPA	513±18	461±21	-52±16	0.004	-18±24	0.458
	PR+CBT	545±19	511±22	-34±18	0.065		
Light time (min/day)	PR+CBT+BPA	158±12	148±10	-10±10	0.306	-3±14	0.805
	PR+CBT	142±13	135±11	-7±10	0.529		
MVPA (min/day)	PR+CBT+BPA	6±2	9±2	4±1	0.013	2±2	0.307
	PR+CBT	6±2	7±2	2±2	0.305		
C-PPAC Total score	PR+CBT+BPA	47±3	61±9	14±2	0.001	10±3	0.002
	PR+CBT	58±7	62±3	4±3	0.192		
C-PPAC Difficulty score	PR+CBT+BPA	43±4	63±4	20±3	0.001	13±4	0.003
	PR+CBT	52±4	59±4	7±3	0.033		
C-PPAC Amount score	PR+CBT+BPA	44±4	63±4	19±3	0.001	14±4	0.005
	PR+CBT	53±4	59±4	6±3	0.033		

Table 2. Change in PA outcome measures in the PR+CBT+BPA (n = 17) and PR+CBT (n = 15) interve¹ interve¹ ntions.

 $Abbreviations: C-PPAC = Clinical \ visit-PROactive \ physical \ activity \ in \ COPD, \ Mins = Minutes, \ PA = Physical \ activity, \ PR = Pulmonary \ Rehabilitation, \ VMU = Vector \ Magnitude \ Mu = Vector \$

Units. Values are mean±SD. Within and between group differences are reported with 95% confidence intervals (CI). *Clinically important improvement

Table 3. Change in exercise capacity, muscular strength/endurance, QoL and anxiety and depression outcome measures in the PR+CBT+BPA (n = 17) and PR+CBT (n = 15) interventions.

$\begin{array}{c c c c c c c c c c c c c c c c c c c $		Group	Baseline	Post PR	Within Group Mean Difference	P value	Between Group Mean Difference	P value
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	6MWD (m)	PR+CBT+BPA	276±22	339±18	63±15	< 0.001	33±20	0.118
$\begin{tabular}{ c c c c c c c c c c c c c c c c c c c$		PR+CBT	259±23	289±19	30±15	0.044		
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	G (kg)	PR+CBT+BPA	18.6±1.5	19.8±1.6	1.2±2.3	0.595	3.0±1.1	0.003
$\begin{tabular}{ c c c c c c c c c c c c c c c c c c c$		PR+CBT	23.4±1.7	21.1±1.8	-2.2±2.5	0.383		
	MVC (kg)	PR+CBT+BPA	22.5±1.6	27.4±1.7	4.9±1.0	< 0.001	1.5±1.2	0.342
$\begin{tabular}{ c c c c c c c c c c c } \hline PR+CBT & 9\pm1 & 11\pm1 & 2\pm1 & 0.003 \\ \hline PR+CBT+BPA & 3.1\pm0.3 & 2.6\pm0.3 & -0.5\pm0.2 & 0.034 & -0.8\pm0.3 \\ \hline PR+CBT & 3.2\pm0.3 & 3.5\pm0.3 & 0.3\pm0.2 & 0.206 \\ \hline CCQ (S) & PR+CBT+BPA & 2.9\pm0.2 & 2.4\pm0.3 & -0.5\pm0.2 & 0.023 & -0.5\pm0.4 \\ \hline PR+CBT & 3.4\pm0.2 & 3.4\pm0.3 & 0.0\pm0.3 & 0.973 \\ \hline CCQ (F) & PR+CBT+BPA & 2.9\pm0.3 & 2.6\pm0.3 & -0.3\pm0.3 & 0.257 & -0.2\pm0.4 \\ \hline PR+CBT & 3.2\pm0.3 & 3.1\pm0.3 & -0.1\pm0.3 & 0.778 \\ \hline CCQ (M) & PR+CBT+BPA & 2.7\pm0.4 & 1.6\pm0.4 & -1.1\pm0.3 & 0.002 & -1.1\pm0.5 \\ \hline PR+CBT & 2.4\pm0.4 & 2.4\pm0.4 & 0.0\pm0.4 & 0.938 \\ \hline CAT & PR+CBT+BPA & 2.9\pm1 & 31\pm1 & 2\pm1 & 0.519 & -2\pm2 \\ \hline PR+CBT & 2.5\pm1 & 2.9\pm1 & 4\pm2 & 0.020 \\ \hline HADS (A) & PR+CBT+BPA & 13\pm1 & 10\pm1 & -3\pm1 & 0.002 & -2\pm1 \\ \hline PR+CBT & 11\pm1 & 10\pm1 & -1\pm1 & 0.277 \\ \hline HADS (D) & PR+CBT+BPA & 11\pm1 & 8\pm1 & -3\pm1 & <0.001 & -1\pm1 \\ \hline PR+CBT & 10\pm2 & 8\pm1 & -2\pm1 & 0.003 \\ \hline \end{tabular}$		PR+CBT	21.2±1.7	24.6±1.8	3.4±1.1	0.004		
$\begin{array}{c} {\rm CCQ}({\rm T}) & \begin{array}{c} {\rm PR+CBT+BPA} & 3.1\pm 0.3 & 2.6\pm 0.3 & -0.5\pm 0.2 & 0.034 & -0.8\pm 0.3 \\ \hline {\rm PR+CBT} & 3.2\pm 0.3 & 3.5\pm 0.3 & 0.3\pm 0.2 & 0.206 \\ \hline {\rm CCQ}({\rm S}) & \begin{array}{c} {\rm PR+CBT+BPA} & 2.9\pm 0.2 & 2.4\pm 0.3 & -0.5\pm 0.2 & 0.023 & -0.5\pm 0.4 \\ \hline {\rm PR+CBT} & 3.4\pm 0.2 & 3.4\pm 0.3 & 0.0\pm 0.3 & 0.973 \\ \hline {\rm PR+CBT} & 3.4\pm 0.2 & 3.4\pm 0.3 & 0.0\pm 0.3 & 0.257 & -0.2\pm 0.4 \\ \hline {\rm PR+CBT} & 3.2\pm 0.3 & 2.6\pm 0.3 & -0.3\pm 0.3 & 0.257 & -0.2\pm 0.4 \\ \hline {\rm PR+CBT} & 3.2\pm 0.3 & 3.1\pm 0.3 & -0.1\pm 0.3 & 0.778 \\ \hline {\rm CCQ}({\rm M}) & \begin{array}{c} {\rm PR+CBT+BPA} & 2.9\pm 0.3 & 2.6\pm 0.3 & -0.3\pm 0.3 & 0.020 & -1.1\pm 0.5 \\ \hline {\rm PR+CBT} & 3.2\pm 0.3 & 3.1\pm 0.3 & -0.1\pm 0.3 & 0.002 & -1.1\pm 0.5 \\ \hline {\rm PR+CBT} & 2.4\pm 0.4 & 2.4\pm 0.4 & 0.0\pm 0.4 & 0.938 \\ \hline {\rm CAT} & \begin{array}{c} {\rm PR+CBT+BPA} & 2.9\pm 1 & 31\pm 1 & 2\pm 1 & 0.519 & -2\pm 2 \\ \hline {\rm PR+CBT} & 2.5\pm 1 & 29\pm 1 & 4\pm 2 & 0.020 \\ \hline {\rm RADS}({\rm A}) & \begin{array}{c} {\rm PR+CBT+BPA} & 15\pm 1 & 10\pm 1 & -3\pm 1 & 0.002 & -2\pm 1 \\ \hline {\rm PR+CBT} & 11\pm 1 & 10\pm 1 & -1\pm 1 & 0.277 \\ \hline {\rm HADS}({\rm D}) & \begin{array}{c} {\rm PR+CBT+BPA} & 11\pm 1 & 8\pm 1 & -3\pm 1 & <0.001 & -1\pm 1 \\ \hline {\rm PR+CBT} & 10\pm 2 & 8\pm 1 & -2\pm 1 & 0.003 \\ \end{array} \right.$	t to Stand (reps)	PR+CBT+BPA	9±1	12±1	3±1	< 0.001	1±1	0.023
$\begin{tabular}{ c c c c c c c } \hline PR+CBT & 3.2\pm0.3 & 3.5\pm0.3 & 0.3\pm0.2 & 0.206 \\ \hline CCQ (S) & $PR+CBT+BPA & 2.9\pm0.2 & 2.4\pm0.3 & -0.5\pm0.2 & 0.023 & -0.5\pm0.4 \\ \hline PR+CBT & 3.4\pm0.2 & 3.4\pm0.3 & 0.0\pm0.3 & 0.973 \\ \hline PR+CBT & 3.2\pm0.3 & 2.6\pm0.3 & -0.3\pm0.3 & 0.257 & -0.2\pm0.4 \\ \hline PR+CBT & 3.2\pm0.3 & 3.1\pm0.3 & -0.1\pm0.3 & 0.778 \\ \hline CCQ (M) & $PR+CBT+BPA & 2.7\pm0.4 & 1.6\pm0.4 & -1.1\pm0.3 & 0.002 & -1.1\pm0.5 \\ \hline PR+CBT & 2.4\pm0.4 & 2.4\pm0.4 & 0.0\pm0.4 & 0.938 \\ \hline CAT & $PR+CBT+BPA & 29\pm1 & 31\pm1 & 2\pm1 & 0.519 & -2\pm2 \\ \hline PR+CBT & 2.5\pm1 & 29\pm1 & 4\pm2 & 0.020 \\ \hline PR+CBT & 2.5\pm1 & 29\pm1 & 4\pm2 & 0.020 \\ \hline PR+CBT & 11\pm1 & 10\pm1 & -3\pm1 & 0.002 & -2\pm1 \\ \hline PR+CBT & 11\pm1 & 10\pm1 & -1\pm1 & 0.277 \\ \hline HADS (D) & $PR+CBT+BPA & 11\pm1 & 8\pm1 & -3\pm1 & <0.001 & -1\pm1 \\ \hline PR+CBT & 10\pm2 & 8\pm1 & -2\pm1 & 0.003 \\ \hline \end{tabular}$		PR+CBT	9±1	11±1	2±1	0.003		
$\begin{array}{c} \mbox{CCQ (S)} & \mbox{PR+CBT+BPA} & 2.9\pm0.2 & 2.4\pm0.3 & -0.5\pm0.2 & 0.023 & -0.5\pm0.4 \\ \hline \mbox{PR+CBT} & 3.4\pm0.2 & 3.4\pm0.3 & 0.0\pm0.3 & 0.973 \\ \hline \mbox{CCQ (F)} & \mbox{PR+CBT+BPA} & 2.9\pm0.3 & 2.6\pm0.3 & -0.3\pm0.3 & 0.257 & -0.2\pm0.4 \\ \hline \mbox{PR+CBT} & 3.2\pm0.3 & 3.1\pm0.3 & -0.1\pm0.3 & 0.778 \\ \hline \mbox{PR+CBT} & 3.2\pm0.3 & 3.1\pm0.3 & -0.1\pm0.3 & 0.778 \\ \hline \mbox{CCQ (M)} & \mbox{PR+CBT} & 2.7\pm0.4 & 1.6\pm0.4 & -1.1\pm0.3 & 0.002 & -1.1\pm0.5 \\ \hline \mbox{PR+CBT} & 2.4\pm0.4 & 2.4\pm0.4 & 0.0\pm0.4 & 0.938 \\ \hline \mbox{CAT} & \mbox{PR+CBT} & 25\pm1 & 29\pm1 & 4\pm2 & 0.020 \\ \hline \mbox{PR+CBT} & 25\pm1 & 29\pm1 & 4\pm2 & 0.020 \\ \hline \mbox{PR+CBT} & 15\pm1 & 10\pm1 & -3\pm1 & 0.002 & -2\pm1 \\ \hline \mbox{PR+CBT} & 11\pm1 & 10\pm1 & -1\pm1 & 0.277 \\ \hline \mbox{HADS (D)} & \mbox{PR+CBT+BPA} & 11\pm1 & 8\pm1 & -3\pm1 & <0.001 & -1\pm1 \\ \hline \mbox{PR+CBT} & 10\pm2 & 8\pm1 & -2\pm1 & 0.003 \\ \hline \mbox{CAT} & \mbox{OO} & \ \mbox{CAT} & \mbox{CAT} &$	CQ (T)	PR+CBT+BPA	3.1±0.3	2.6±0.3	-0.5 ± 0.2	0.034	-0.8±0.3	0.020
$\begin{tabular}{ c c c c c c c } \hline PR+CBT & 3.4\pm0.2 & 3.4\pm0.3 & 0.0\pm0.3 & 0.973 \\ \hline PR+CBT+BPA & 2.9\pm0.3 & 2.6\pm0.3 & -0.3\pm0.3 & 0.257 & -0.2\pm0.4 \\ \hline PR+CBT & 3.2\pm0.3 & 3.1\pm0.3 & -0.1\pm0.3 & 0.778 \\ \hline PR+CBT & 3.2\pm0.3 & 3.1\pm0.3 & -0.1\pm0.3 & 0.002 & -1.1\pm0.5 \\ \hline PR+CBT & 2.4\pm0.4 & 2.4\pm0.4 & 0.0\pm0.4 & 0.938 \\ \hline PR+CBT & 2.4\pm0.4 & 2.4\pm0.4 & 0.0\pm0.4 & 0.938 \\ \hline CAT & $PR+CBT+BPA$ & 29 ± 1 & 31 ± 1 & 2 ± 1 & 0.519 & -2 ± 2 \\ \hline PR+CBT & 25 ± 1 & 29 ± 1 & 4 ± 2 & 0.020 \\ \hline HADS (A) & $PR+CBT+BPA$ & 13 ± 1 & 10 ± 1 & -3 ± 1 & 0.002 & -2 ± 1 \\ \hline PR+CBT & 11 ± 1 & 10 ± 1 & -3 ± 1 & 0.002 & -2 ± 1 \\ \hline PR+CBT & 11 ± 1 & 10 ± 1 & -3 ± 1 & 0.002 & -2 ± 1 \\ \hline HADS (D) & $PR+CBT+BPA$ & 11 ± 1 & 8 ± 1 & -3 ± 1 & <0.001 & -1 ± 1 \\ \hline PR+CBT & 10 ± 2 & 8 ± 1 & -2 ± 1 & 0.003 \\ \hline \end{tabular}$		PR+CBT	3.2±0.3	3.5±0.3	0.3±0.2	0.206		
$\begin{array}{c c} CCQ \left(F \right) & \begin{array}{c} PR+CBT+BPA & 2.9\pm 0.3 & 2.6\pm 0.3 & -0.3\pm 0.3 & 0.257 & -0.2\pm 0.4 \\ \hline PR+CBT & 3.2\pm 0.3 & 3.1\pm 0.3 & -0.1\pm 0.3 & 0.778 \\ \hline PR+CBT & 2.7\pm 0.4 & 1.6\pm 0.4 & -1.1\pm 0.3 & 0.002 & -1.1\pm 0.5 \\ \hline PR+CBT & 2.4\pm 0.4 & 2.4\pm 0.4 & 0.0\pm 0.4 & 0.938 \\ \hline CAT & \begin{array}{c} PR+CBT+BPA & 29\pm 1 & 31\pm 1 & 2\pm 1 & 0.519 & -2\pm 2 \\ \hline PR+CBT & 25\pm 1 & 29\pm 1 & 4\pm 2 & 0.020 \\ \hline PR+CBT & 25\pm 1 & 29\pm 1 & 4\pm 2 & 0.020 \\ \hline PR+CBT & 11\pm 1 & 10\pm 1 & -3\pm 1 & 0.002 & -2\pm 1 \\ \hline PR+CBT & 11\pm 1 & 10\pm 1 & -1\pm 1 & 0.277 \\ \hline PR+CBT & 11\pm 1 & 10\pm 1 & -3\pm 1 & <0.001 & -1\pm 1 \\ \hline PR+CBT & 10\pm 2 & 8\pm 1 & -3\pm 1 & <0.003 \\ \hline \end{array}$	CQ (S)	PR+CBT+BPA	2.9±0.2	2.4±0.3	-0.5±0.2	0.023	-0.5±0.4	0.655
PR+CBT 3.2±0.3 3.1±0.3 -0.1±0.3 0.778 CCQ (M) PR+CBT+BPA 2.7±0.4 1.6±0.4 -1.1±0.3 0.002 -1.1±0.5 PR+CBT 2.4±0.4 2.4±0.4 0.0±0.4 0.938 0.778 CAT PR+CBT+BPA 29±1 31±1 2±1 0.519 -2±2 PR+CBT 25±1 29±1 4±2 0.020 -2±1 HADS (A) PR+CBT 13±1 10±1 -3±1 0.002 -2±1 HADS (D) PR+CBT+BPA 11±1 8±1 -3±1 <0.001		PR+CBT	3.4±0.2	3.4±0.3	0.0±0.3	0.973		
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	CQ (F)	PR+CBT+BPA	2.9±0.3	2.6±0.3	-0.3±0.3	0.257	-0.2±0.4	0.564
$\begin{tabular}{ c c c c c c c } \hline PR+CBT & 2.4\pm0.4 & 2.4\pm0.4 & 0.0\pm0.4 & 0.938 \\ \hline CAT & $PR+CBT+BPA$ & 29 ± 1 & 31 ± 1 & 2 ± 1 & 0.519 & -2 ± 2 \\ \hline PR+CBT & 25 ± 1 & 29 ± 1 & 4 ± 2 & 0.020 \\ \hline HADS (A) & $PR+CBT+BPA$ & 13 ± 1 & 10 ± 1 & -3 ± 1 & 0.002 & -2 ± 1 \\ \hline PR+CBT & 11 ± 1 & 10 ± 1 & -1 ± 1 & 0.277 \\ \hline HADS (D) & $PR+CBT+BPA$ & 11 ± 1 & 8 ± 1 & -3 ± 1 & <0.001 & -1 ± 1 \\ \hline PR+CBT & 10 ± 2 & 8 ± 1 & -2 ± 1 & 0.003 \\ \hline \end{tabular}$		PR+CBT	3.2±0.3	3.1±0.3	-0.1±0.3	0.778		
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	CQ (M)	PR+CBT+BPA	2.7 ± 0.4	1.6±0.4	-1.1±0.3	0.002	-1.1±0.5	0.034
$\begin{tabular}{ c c c c c c c c c c c c c c c c c c c$		PR+CBT	$2.4{\pm}0.4$	$2.4{\pm}0.4$	0.0 ± 0.4	0.938		
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	АT	PR+CBT+BPA	29±1	31±1	2±1	0.519	-2±2	0.092
PR+CBT 11±1 10±1 -1±1 0.277 HADS (D) PR+CBT+BPA 11±1 8±1 -3±1 <0.001		PR+CBT	25±1	29±1	4±2	0.020		
HADS (D) PR+CBT+BPA 11±1 8±1 -3±1 <0.001 -1±1 PR+CBT 10±2 8±1 -2±1 0.003	ADS (A)	PR+CBT+BPA	13±1	10±1	-3±1	0.002	-2±1	0.137
PR+CBT 10±2 8±1 -2±1 0.003		PR+CBT	11±1	10±1	-1±1	0.277		
	ADS (D)	PR+CBT+BPA	11±1	8±1	-3±1	< 0.001	-1±1	0.125
MRC PR+CBT+BPA 3±1 3±1 0±1 0.302 0±1		PR+CBT	10±2	8±1	-2±1	0.003		
	RC	PR+CBT+BPA	3±1	3±1	0±1	0.302	0±1	0.205
PR+CBT 3±1 3±1 0±1 0.208		PR+CBT	3±1	3±1	0±1	0.208		

Abbreviations: 6MWT = Six Minute Walk Test, HG = Hand grip, QMVC = Quadriceps Muscle Voluntary Capacity, CCQ = Clinical COPD Questionnaire, T = Total, S = Symptoms, F = Functional, M = Mental, CAT = COPD Assessment Test, HADS = Hospital Anxiety and Depression Scale, A = Anxiety, D = Depression, MRC = Medical Research Council Dyspnea scale, m = Metres, PA = Physical activity, PR = Pulmonary Rehabilitation. Values are mean±SD. Within and between group differences are reported with 95% confidence intervals (CI). *Clinically important improvement.

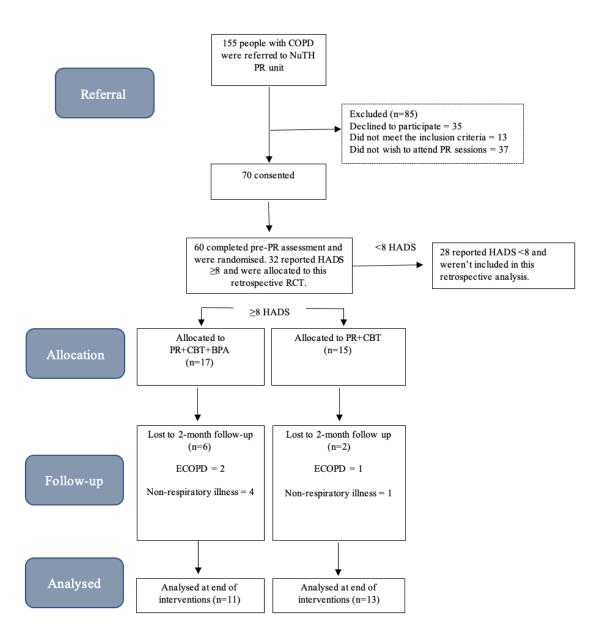


Figure 1. Consolidation standards of Reporting Trials diagram of the study. ECOPD: exacerbation of COPD.

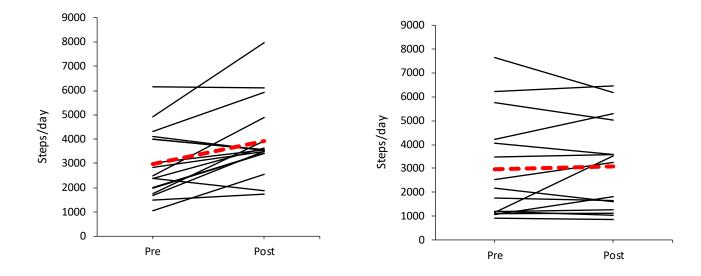


Figure 2. Individual responses to the PR+CBT+BPA and CBT+PR for changes in steps/day.

PR+CBT+BPA

PR+CBT

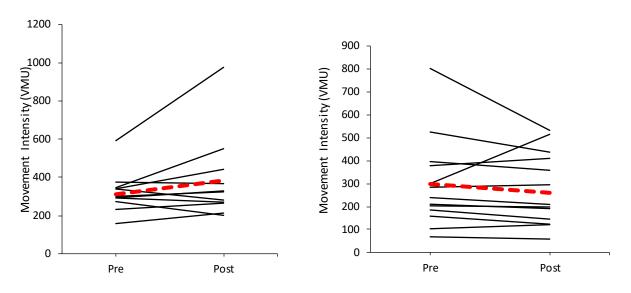


Figure 3. Individual responses to the PR+CBT+BPA and CBT+PR for changes in movement intensity (VMU).