Official title:

PACE - Physical Activity in COPD Using E-Health: Effectiveness of a Personalised eHealth Platform Integrated into Pulmonary Rehabilitation to Increase Physical Activity in Patients with COPD - a Randomized Controlled Trial

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PACE - Effectiveness of Physical Activity Coaching using E-Health in patients with COPD: a randomized controlled trial

ABSTRACT

Background: Physical inactivity is the 4th leading risk factor for death worldwide, being particularly relevant in patients with COPD, since it is related to increased risk for exacerbations, hospitalisations and mortality. Pulmonary rehabilitation (PR) is an evidence-based intervention known to optimise patients' symptoms and functional performance and reduce health-related costs. However, its influence on patients' increase and maintenance of PA is modest. Hence, there is an urgent need for strategies to optimise PA outcomes during/after PR. Personalised coaching through mobile apps may be an answer, as they are ubiquitous in people's everyday lives.

Objective: This study aims to assess the effectiveness of an eHealth PA coaching intervention in PA levels of patients with COPD, during and after PR.

Methods: An 8-month, two-arm, parallel-group, assessor blinded, multicentre randomized controlled study will be conducted. Participants randomized to the control group will attend the PR program for 10 weeks. Participants randomized to the intervention group will also attend the same PR and an eHealth PA coaching intervention after week 5 of PR until 6 months after end of PR. This eHealth intervention includes a mobile app, connected to a smartband, for patients and web app for healthcare professionals, through PA goal setting/ progression, notifications and PA promotion will occur. The number of daily steps will be the primary outcome, assessed through accelerometry, and health-related outcomes will be also evaluated as dyspnoea, impact of disease, quality of life, PA self-efficacy and exercise capacity. The assessment will take place in weeks 0, 5, 10 of PR and 3- and 6-months after end of PR.

Results: The previous pilot-study has shown this PA coaching intervention is acceptable and feasible in patients with COPD attending PR program. The recruitment to the trial will start in November 2024. We expect to start data collection also in November 2024 and expect it to last for approximately 8 months. We expect to complete data collection by mid-2025 and plan the dissemination of the results subsequently.

Conclusions: To our knowledge, this is the first study investigating a combination of an eHealth PA coaching intervention and a PR in patients with COPD. We will investigate the effectiveness of the proposed intervention and provide evidence to further guide new approaches to PA promotion in COPD.

Trial registration: ClinicalTrials.gov identifier: X

Keywords: physical activity, COPD, eHealth, pulmonary rehabilitation

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a highly prevalent disease which imposes a great burden on the healthcare systems and is a major cause of long-term disability [1]. Physical inactivity is a strong risk factor for mortality worldwide [2], being particularly relevant in patients with COPD. Patients with COPD are markedly inactive, and inactivity is related to increased risk of exacerbations, hospitalisations and mortality [2]. Thus, improving physical activity (PA) levels in these patients is a global priority [1]. Pulmonary rehabilitation (PR) is a non-pharmacological and evidence-based intervention known to improve symptomatology and functional performance in patients with COPD [3-5]; however, its benefits tend to decrease over time [6]. Furthermore, previous studies have found inconsistent results on the impact of exercise-based PR on patients' PA levels, suggesting that additional behavioural interventions are needed to promote active lifestyles [7].

There is some evidence that behaviour change interventions may increase PA in patients with COPD [8]. The Digital Health Interventions could scale and tailor lifestyle behaviour support to individuals in need at sustainable costs [9], since the frequent personal coaching by human healthcare professionals is neither scalable nor financially sustainable by healthcare systems [10]. Thus, PA coaching and monitoring through Information and Communication

Technologies (eHealth) such as mobile applications (apps) may be a solution, since their use is increasingly common in everyday life [11] and are embedded into the healthcare systems [12].

Using eHealth for PA coaching could promote sustainable PA behaviours in these patients, as mobile apps can monitor PA in real-time, allowing automated and continuous self-monitoring and feedback on the PA performed [13], enabling the burdenless measurement of activity with acceptable accuracy [14], and continuous access to recorded data (longitudinally and in real time) [13]. Additionally, it may be available to people living in remote areas or in areas where access to healthcare providers is limited, reducing access inequities [15]. Integrating an eHealth platform with personalised PA coaching during PR, allowing clinicians to early detect and intervene in case of low PA adherence [15], may be a useful strategy to help patients to be more physically active.

The aim of this randomized controlled trial (RCT) is to assess the effectiveness of a PA coaching intervention using eHealth, during and after PR, on patients' PA levels and health-related outcomes.

METHODS

Trial design

This will be an 8-month, two-arm, parallel-group, assessor blinded, multicentre randomized controlled study. The study has been registered and approved by Clinical Trials (number XXX) and will follow the Consolidated Standards of Reporting Trials Statement [16] and the guidelines for reporting of eHealth interventions [17]. The Ethics Committee of the institutions involved, i.e., Local Health Unit of Baixo Mondego, Coimbra and North Lisbon will approve the study and written informed consent will be obtained from the participants prior to the data collection. The illustration of the design of this clinical randomized trial in Figure 1.

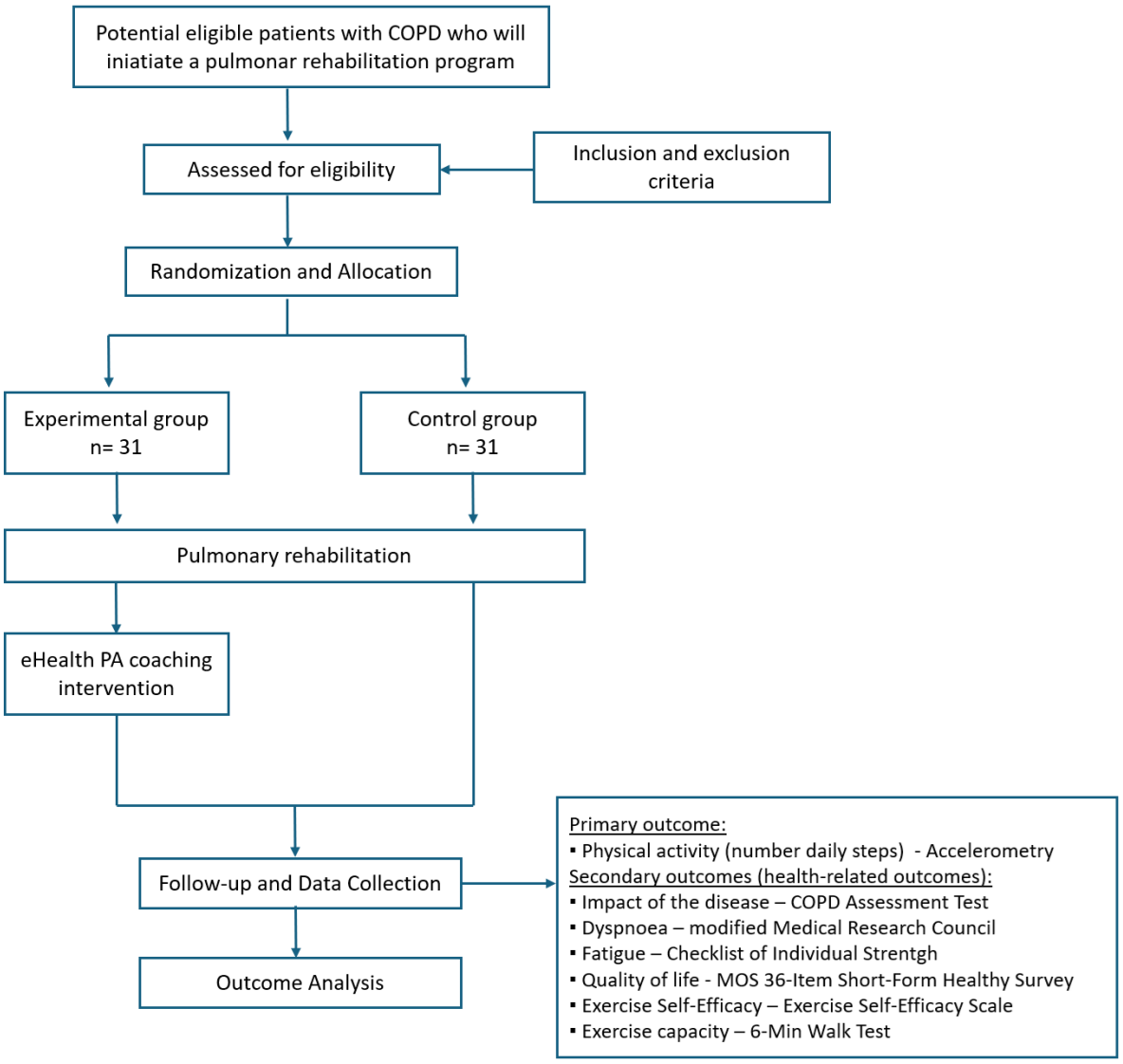

Figure 1 – Design of the randomized controlled trial.

Eligibility criteria

Patients will be recruited from the hospitals in the central region of the country collaborating in the study, specifically Local Health Unit of Baixo Mondego, Coimbra and North Lisbon, according to the following eligibility criteria: age > 40 years old, diagnosis of COPD according to GOLD criteria [1], clinically stable (i.e., with no exacerbations in previous month), being enrolled in a pulmonary rehabilitation program, having a smartphone with access to internet and be able to understand and provide informed consent. The exclusion criteria will be simultaneous participation in another behavioural modification program; having any clinical condition that precludes participation in a PA intervention (e.g., severe musculoskeletal or

neurological disorders, unstable cardiovascular disease); other primary respiratory disease; and/or history of recent neoplasia (including last treatment) in the previous year.

Procedures

The physicians responsible for the PR program in each hospital will identify the eligible participants and briefly explain them the study. Those interested to participate will then be contacted by the researcher who will explain the study aims and procedures (data collection, dates and intervention delivery), confirm their eligibility and ask their willingness to participate. Reasons for not participating will be recorded. Patients who agree to participate will sign a written informed consent prior to any data collection.

All participants will attend the PR program for 10 weeks (approximately 20 sessions) and will be assessed 5 times during study period: T0 (baseline assessment, one week before PR), T1 (week 5 of PR), T2 (week 10 of PR), T3 (12 weeks after PR) and T4 (24 weeks after PR). The first assessment includes a questionnaire with sociodemographic information and health-related information (i.e., age, sex, educational level, occupational status, smoking history, comorbidities, exacerbations history, medication and body mass index), preferred physical activities and questions about the use of mobile devices and apps (i.e., what tasks do patients perform most frequently, namely, receiving/sending text messages, using GPS, listening to music, using apps, accessing social media…). Then patients will complete clinical questionnaires regarding symptoms, health-related quality of life and PA self-efficacy. The lung function and exercise capacity will be also assessed. PA will be objectively measured through accelerometry.

In week 5 of PR (T1), the experimental group will be provided with a mobile app (Fitrockr Hub App, Fitrockr Health Solutions, Berlin, Germany) and a smartband (Garmin Vivosmart 4, Arkansas, United States) that will monitor their daily step count. After one week of monitoring without PA goals prescribed in the app, personal PA goals will be retrieved in the coaching app - more information about the PA coaching intervention is provided below. The researcher responsible for implementing the intervention will contact patients of the experimental group on a weekly basis to confirm whether the previous week goal was achieved, set the next goal with the patient, identify barriers to PA and strategies to overcome them (if applicable), and address any technical issues with the app. The schedule of enrolments, interventions and assessment moments is shown in

Table 1 - The schedule of enrolments, interventions and assessment moments.

Study period							
	Baseline assessment (T0)	**Start of PR**	**Middle of PR (T1)**	**End of PR (T2)**	**3-month follow-up (T3)**	**6-month follow-up (T4)**	**Group**
Week	**-1**	**0**	**5**	**10**	**22**	**34**	
Interventions							
Experimental Group		Pulmonary Rehabilitation					EG
			eHealth PA coaching intervention				
PA coaching app + smartband			✓	✓	✓	✓	EG
Goal setting (every week after T1)			✓	✓	✓	✓	EG
Control Group		Pulmonary Rehabilitation					CG
			-				
Assessments							
Sociodemographic information + lung function (spirometry)	✓						EG/CG
Impact of the disease (CAT)	✓		✓	✓	✓	✓	EG/CG
Dyspnoea (mMRC)	✓		✓	✓	✓	✓	EG/CG
Fatigue (CIS20)	✓		✓	✓	✓	✓	EG/CG
Self-Efficacy (Physical Activity Self-Efficacy Scale)	✓		✓	✓	✓	✓	EG/CG
Health-related quality of life (SF-36)	✓		✓	✓	✓	✓	EG/CG
PA (accelerometry)	✓		✓	✓	✓	✓	EG/CG
Exercise capacity (6MWT)	✓		✓	✓	✓	✓	EG/CG

Legend: 6MWT, Six-minute Walk Test; CAT, COPD Assessment Test; CE, Control Group; CIS-20, Checklist of Individual Strength; EG, Experimental Group; mMRC, modified Medical Research Council scale; PR, Pulmonary Rehabilitation; SF-36, The MOS 36-Item Short-Form Healthy Survey.

Randomization and blinding

After providing the informed consent, patients will be randomized into the experimental or control groups in a 1:1 ratio. Random serial numbers will be generated through the Research Randomizer (available at https://www.sealedenvelope.com/simple-randomiser/v1/lists), using varying block sizes of 2 and 4 and stratified by centre, and allocation codes will be kept in sealed opaque envelopes. This procedure will be conducted by a researcher who will not directly participate in the recruitment, data collection and the implementation of the intervention.

Due to nature of the intervention (PA coaching intervention), blinding of participants and the researcher implementing it will not be possible. Nevertheless, the outcome assessor (i.e., researcher responsible for assessing participants in the study visits) will be blinded.

Sample size calculation

The sample size was determined using G*Power (version 3.1.9.7) [18] for a repeated measures design with a within-between interaction. The analysis was based on an effect size (f) of 0.178, derived from a clinically meaningful difference (MCID) of 1100 steps/day [19] and a standard deviation of 3168.3 steps/day [20], and considered the inclusion of 2 groups and 5 repeated measurements over time. The significance level (α) was set at 0.05 (two-tailed), and the power ($1-\beta$) at 0.80. A correlation among repeated measures (r) of 0.5 and a nonsphericity correction (ϵ) of 1.0 were applied to ensure a conservative calculation. Based on these parameters, the total sample size required was calculated to be 40 participants. Considering that previous studies have shown dropout rates between 20% and 39% [21, 22], the sample size was adjusted for an anticipated 30% dropout rate, using the formula: sample size/(1-dropout rate). Thus, the final sample size required to maintain adequate statistical power for detecting clinically meaningful changes in the primary outcome is 57 participants.

Interventions

Pulmonary rehabilitation

PR is defined as “a comprehensive intervention based on thorough patient assessment followed by patient-tailored therapies that include, but are not limited to exercise training,

education, self-management intervention aiming at behaviour change, designed to improve the physical and psychological condition of people with chronic respiratory disease and to promote the long-term adherence to health-enhancing behaviours" [23]. All participants (from experimental and control group) will attend a similar PR program, regarding exercise training and education component, particularly the session on PA importance and recommendations, which will be held before T1 (i.e., before receiving the PA coaching intervention). A detailed description of the PR programs implemented in each collaborating hospital can be found in supplementary material 2.

PA coaching intervention using eHealth

eHealth platform

The eHealth platform that will be used in the PA coaching intervention will be the Fitrockr platform (Fitrockr Health Solutions, Berlin, Germany) which consists of two apps – a web app for healthcare professionals and a mobile app (Fitrockr Hub App) for patients. The Fitrockr Hub App, connected to a Garmin VivoSmart 4 smartband (Garmin, Kansas, United States), enables tailoring PA coaching to each patient by tracking PA (i.e., steps), monitoring patients' adherence to predefined PA goals, enabling individualised notifications on patient's performance based on the fulfilment of their personal goals. The synchronization between mobile app and smartband will be conducted by patients twice a day, every day, with a manual click in a specific button in the app (if the patient forgets to synchronize on a given day, the PA data is not lost, since is recorded in the next synchronization).

The web app for healthcare professionals (here represented by the researcher) can monitor patients' daily steps to define and/or change patients' individualised goals, which will then appear on the homepage of the mobile app. Through the web page, the healthcare professionals can also insert new patients, prescribe personalised PA goals for each patient, monitor their daily PA and check whether patients meet their prescribed goals.

PA coaching intervention

In the 5-week PR (T1), all participants will be assessed for the second time and participants in the experimental group will be asked to wear the Fitrockr Hub App connected to the Garmin's smartband every day during the study period and instructions on its use will be also provided. During the first week, no PA goals will be prescribed in the app since the first PA goal will be

prescribed according to their baseline PA levels. After that, the first goal will be set through a phone call and the personalisation of goal prescription will based on an algorithm considering the performance in the previous week (i.e., average number of daily steps during the last 7 days) and easiness question (i.e., “On a scale of 0-10, how easy was it for you to achieve this value last week?”) (Figure 2). The “easiness” value will be translated into percentage of improvement and patients will be asked about their confidence to increase that value to the average steps reached in the previous week, using a ‘yes’ or ‘no’ question. To avoid risk of injuries and to ensure tolerability, the increases in PA goals will not exceed the maximum of 10% [24]. If patient shows confidence to increase, the extra number of steps will be added to their previous average steps; if the patient does not show confidence to increase, the researcher will ask for the reasons, identifying possible barriers to PA and strategies to overcome them (see supplementary material 1 [25]). After that, if confidence level of patient increases, an intermediate goal increase will be negotiated; if the patient does not show any confidence, then the average steps of the previous week will be used as the first goal.

The PA goals will be displayed in the Fitrockr Hub App where patients will receive daily feedback on their PA progress and notifications. Patients will receive a daily notification about their goal achievements, at 6PM, giving them the possibility to practice more PA to complete the goal when relevant. During the intervention, patients will also receive personalized notifications sent by the researcher, whenever needed to increase their engagement with PA practice (e.g., notification about bad weather suggesting indoor activities…).

The weekly progression of the PA goals will be based on the algorithm shown below (Figure 3), conducted by phone calls, similarly to the first goal setting. The duration, content and reasons for extra phone calls will be recorded, if they happen.

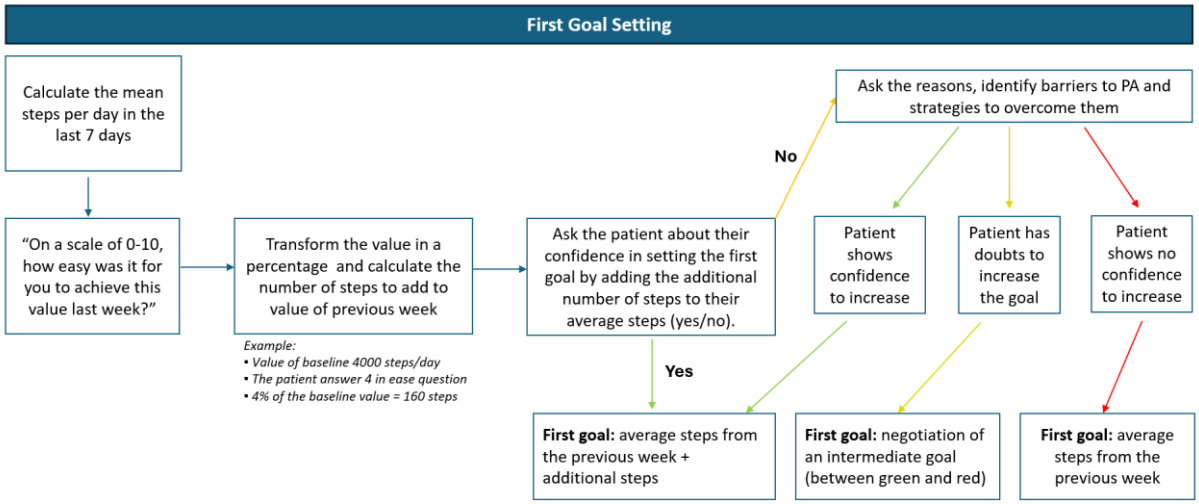

Figure 2 - Algorithm of first goal setting.

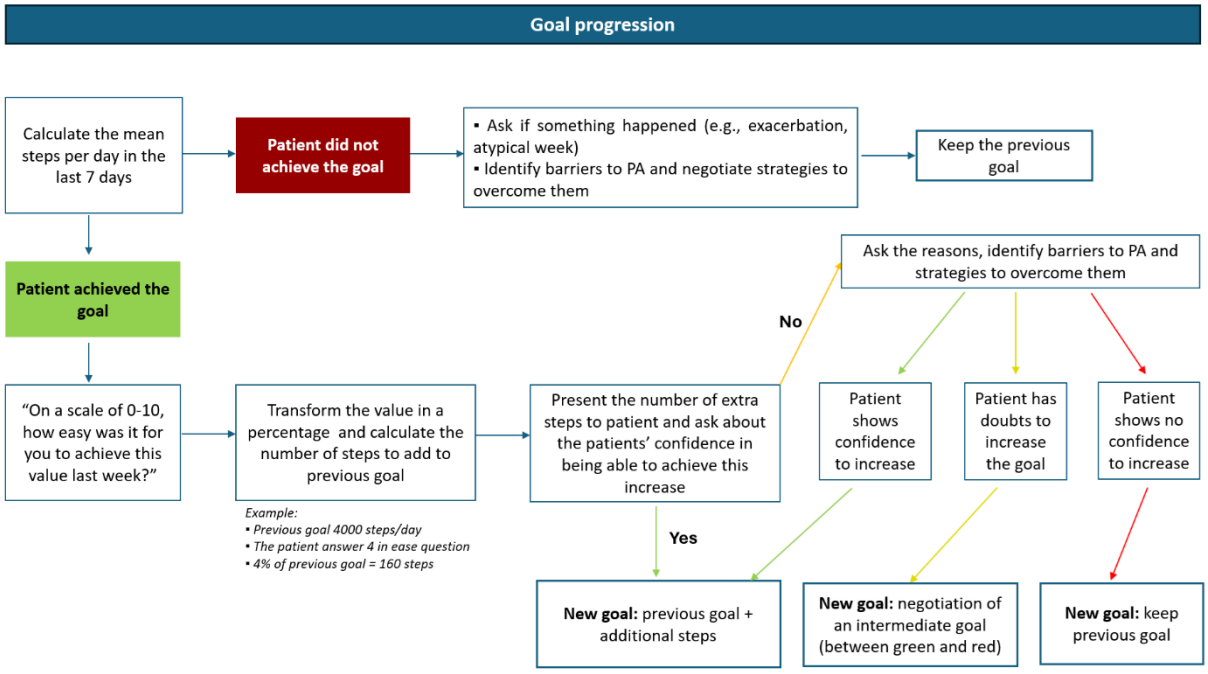

Figure 3 - Algorithm of goal progression.

Since in COPD both physical and behavioural components influence activity levels [5, 26], this intervention incorporated several behaviour changes techniques (BCTs) [27]: 1) goals setting (behaviour) - Negotiated PA goals between the researcher and patient on a weekly basis; 2) problem solving - Identification of barriers to PA practice and possible strategies to overcome them during the telephone calls; 3) Review behaviour goals - Weekly goal revision/progression by the researcher and the patient; 4) Feedback on behaviour - Patients receive feedback about

their PA performance during the intervention, through the app; 5) Self-monitoring of behaviour - Patients synchronize the app with the smartband and observe their PA history (steps, calories and distance) on a daily basis; 6) Information about health and emotional consequences - Patients are informed on the health benefits of PA practice during the first goal setting moment and education session of PR; 7) Behaviour substitution - During intervention, the researcher suggests the substitution of sedentary activities for more active activities of daily living, such as going for a walk instead of sitting while watching television; 8) Habit reversal - During intervention, the researcher advises the patient to replace some activities for more active ones, such as climbing the stairs instead of using the lift; 9) Graded tasks - The PA goals negotiated between the researcher and the patient are based on their PA performance in the previous week, being gradually increased according to patient's confidence and willingness to progress; 10) Social incentive - Patients will receive notifications in the app congratulating them in case of goal achievement and/or with incentives to improve their PA performance; and 11) Verbal persuasion about capability - The healthcare professional, tells the patients that they can successfully increase their PA levels, despite of their disease.

Outcome measures and follow-up

Primary outcome – PA levels

PA will be objectively measured using the triaxial accelerometer Actigraph GT3X+ (Pensacola, FL, US), already validated in COPD [28]. The device collects and stores PA data which can be downloaded and converted into time-stamped PA counts and step counts using specific software (ActiLife 6, version 6.13.3, Pensacola, FL). Patients will be instructed to wear the accelerometer for 7 days on the dominant side of their waist, held by an elastic strap, during waking hours, except for bathing or swimming. A valid day will be defined as a minimum of 8 h of wearing time [29]. Accelerometer-based data will be then downloaded and analysed using the algorithms of Freedson (1998) [30] with 60-s epoch, incorporated in the Actilife software: daily time (in min) spent in light-intensity PA (100–1951 counts-per-minute [CPM]), MPA (1952–5724 CPM), VPA (≥5725 CPM), and a combination of both (MVPA). The number of steps per day and per week will also be collected.

Secondary outcomes – health-related outcomes

Functional exercise capacity

Functional exercise capacity will be measured using 6MWT [31], and predicted values were computed using the equation developed for Portuguese adults [32]. The test will be conducted in a 30-meter corridor according to guidelines from ERS/ATS [33]. Heart rate, blood pressure and peripheral oxygen saturation will be measured before and after the test [34], and symptom scores for dyspnoea and fatigue will be measured by the modified Borg scale [35]. The 6MWT will be performed twice per assessment moment, with more than 30 minutes of interval, and the best result will be used for analysis.

Symptoms

Dyspnoea will be assessed through the modified Medical Research Council (mMRC) dyspnoea scale [36], fatigue through the Checklist of Individual Strength (CIS20) [37] and impact of symptoms on health status with the COPD Assessment Test (CAT) [38].

Quality of life and PA Self-Efficacy

The quality of life will be assessed with MOS Short-Form Health Survey 36 Item v2 (SF-36) [39, 40] and self-efficacy for PA with Physical Exercise Self-Efficacy Scale [41].

Statistical analysis

Data will be analysed using the Statistical Package for Social Sciences (SPSS)® software version 24 (IBM Corp., Armonk, USA) and statistical significance will be considered at $p<0.05$. Descriptive statistics will be used to characterise the sample. Normality of data distribution will be assessed using Kolmogorov-Smirnov test. Chi-square, Mann-Whitney U and *t* tests will be used to compare baseline characteristics between groups, as appropriate. Longitudinal analyses will be conducted according to the intention-to-treat principle - two-way mixed ANOVA will be used to assess differences in time X group interaction, as well as post-hoc analyses when appropriate.

RESULTS

The previous pilot-study has shown this PA coaching intervention is acceptable and feasible in patients with COPD attending PR program. The recruitment to the trial will start in November 2024. We expect to start data collection also in November 2024 and expect it to

last for approximately 8 months. We expect to complete data collection by mid-2025 and plan the dissemination of the results subsequently.

DISCUSSION

Study contributions

To our knowledge, this is the first study investigating a combination of an eHealth PA coaching intervention and a PR in patients with COPD. We will investigate the effectiveness of the proposed intervention and provide evidence to further guide new approaches to PA promotion in COPD.

Strengths and Limitations

Being this a randomized controlled trial, which is considered the "gold standard for evaluating efficacy in clinical research and constitute evidence for medical treatment" [42], the internal and external validity and robustness will be ensured. Also, the methodology of this study is described in detail to minimize any bias throughout the intervention. One limitation of this intervention could be the fact that this type of technological intervention is not suitable for all patients, but this will also be a factor to be analysed according to the results obtained, bearing in mind that in health "one size does not fit all".

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