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# A randomised, controlled, feasibility trial of an online, self-guided breathlessness supportive intervention **(SELF-BREATHE)** for individuals with chronic breathlessness due to advanced disease

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## Abstract

**Introduction:**
SELF-BREATHE is a complex, transdiagnostic, supportive, digital breathlessness intervention co-developed with patients. SELF-BREATHE seeks to build capacity and resilience within health services by improving the lives of people with chronic breathlessness using nonpharmacological, self-management approaches. This study aimed to determine whether SELF-BREATHE is feasible to deliver and acceptable to patients living with chronic breathlessness.

**Methods:**
**Design:** A parallel, two arm, single blind, single centre, randomised controlled mixed-methods feasibility trial with participants allocated to 1) intervention group (SELF-BREATHE) or 2) control group (usual NHS care).
**Setting:** Large multisite NHS Foundation Trust in Southeast London.
**Participants:** Patients living with chronic breathlessness due to advanced malignant or non-malignant disease(s).
**Intervention:** Participants were randomly allocated (1:1) to an online, self-guided, breathlessness, supportive intervention (SELF-BREATHE) and usual care or usual care alone, over six weeks.
***A priori*** **progression criteria**: ≥ 30% of eligible patients given an information sheet consented to participate, ≥ 60% of participants logged on and accessed SELF–BREATHE within 2 weeks, ≥ 70% of patients reported the methodology and intervention as acceptable.

**Results:**
Between January 2021 and January 2022, 52/110 (47%) eligible patients consented and were randomised. Of those randomised to SELF-BREATHE, 19/26 (73%) logged on and used SELF-BREATHE for a mean (SD, range) of 9 (8, 1-33) times over 6-weeks. Thirty-six of the 52 (70%) randomised participants completed and returned the end of study postal questionnaires. SELF-BREATHE users reported it to be acceptable. Post intervention qualitative interviews demonstrated that SELF-BREATHE was acceptable and valued, by users, improving breathlessness during daily life and at points of breathlessness crisis.

**Conclusion:**
These data support the feasibility of moving to a fully powered, efficacy, randomised controlled trial with minor modifications to minimise missing data (i.e., multiple methods for data collection, face-to-face, telephone, video assessment and via post).

## Introduction

Worldwide, more than 75 million people have breathlessness, including more than 90% of the 65 million people with severe lung disease [1], more than 50% of the 10 million with incurable cancer and 50% of the 23 million with heart failure [2, 3]. More than two-thirds of those living with breathlessness have multimorbidity [4]. Breathlessness is a transdiagnostic problem, worsened by social, environmental, and economic problems. The burden of breathlessness on individuals, family, society, and health systems is increasing with population ageing and multimorbidity, amplified by the COVID-19 pandemic, with data suggesting that >40% of COVID-19 survivors have persistent (chronic) breathlessness [5, 6]. Proactive approaches to management of breathlessness are required to build capacity and resilience within health care systems, especially given rising health and social care costs, and workforce challenges.

Clinical management of breathlessness is challenging; optimal pharmacological treatment of the underlying disease is the first step. Disease specific management alone does not guarantee symptom control. Breathlessness increases with disease progression, resulting in poor quality of life [7, 8], increased disability and high health and social care costs [9]. This is often driven by repeated Emergency Department (ED) attendance and hospitalisations [10-12].

There is good evidence for face to face delivered breathlessness supportive services (BSS), which focus on education and non-pharmacological approached to chronic breathlessness self-management [13, 14]. BSS models demonstrate cost effectiveness [15]. However, an implementation gap remains. Traditional face-to-face clinical consultations as standard are being re-examined peri pandemic, and innovative healthcare solutions are sought. Online services may offer one possible solution. Internet connectivity is available to at least 55% of the global population [16]. In the UK, 95% of the adult population are internet users, and this is expected to increase to 98% by 2025 [17]. Global data suggests that internet use and in particular the use of video communication applications have increased exponentially during the COVID-19 pandemic [16]. Increase in internet access and digital literacy in people with chronic respiratory disease during the COVID-19 pandemic has been observed in the UK [18]. Those living with chronic breathlessness due to advanced disease with internet access are willing to use online breathlessness self-management interventions, if available [19].

Disease specific digital supportive online interventions are feasible and acceptable to patients with asthma [20] and COPD [21] , demonstrating improved quality of life [20], inhaler technique and hospital admission rates [20, 21]. However, others have reported challenges with recruiting, retaining and engaging patients pre-pandemic [22]. To date digital interventions have been respiratory disease specific, rather than symptom focused. To address the lack of face-to-face transdiagnostic breathlessness supportive services and online alternatives, SELF-BREATHE was developed.

SELF-BREATHE is a complex, transdiagnostic, breathlessness, supportive digital intervention co-developed with patients following the IDEAS (Integrate, Design, Assess and

Share) and MRC (Medical Research Council) frameworks [19, 23], theoretically underpinned by Leventhal‟s Common-Sense Model of Self-Regulation [24-26]. SELF-BREATHE aims to build capacity and resilience within health services to improve the lives of people living with chronic breathlessness using non pharmacological self-management approaches [19, 23].

The aim of this study was primarily to determine whether a randomised controlled trial of SELF-BREATHE would be feasible to deliver and acceptable to patients living with chronic breathlessness due to advanced disease.

## Study objectives

To determine the feasibility of:

1. **Method of evaluation**: via recruitment and consent rates, randomisation procedure, completeness of data collection.

2. **SELF -BREATHE as an intervention:** number of participants that logged in to SELF-BREATHE, log in frequency and acceptability of SELF-BREATHE.

## Methods

### Methodology
This study followed the MRC framework for developing and evaluating complex interventions [25], MORECARE statement [27] CONSORT statement [36] and the IDEAS (Integrate, DEsign, Assess and Share) framework for the development of digital behavioural change interventions [24].

### Ethical approval
Ethical and local research and development approval was obtained prior to commencing this research (research ethics committee (REC) / health research authority (HRA) reference number 20/LO/1108). The study was registered at www.clinicaltrials. gov (identifier NCT04574050).

### Study design
A single blind (data checker/ inputter) single centre, parallel, two arm randomised controlled trial with participants allocated to either **1)** intervention group (SELF-BREATHE) plus usual national health service (NHS) care) or **2)** control group (usual NHS care). The trial was evaluated using mixed methods (i.e., a RCT and qualitative interviews).

### Setting
Patients were recruited from general and specialist clinics / services (virtual and face to face), at King‟s College Hospital (KCH) NHS Foundation Trust (Denmark Hill and PRU sites)

where there is high prevalence of chronic breathlessness, including,: Integrated Respiratory Teams (IRT), lung cancer, bronchiectasis, and respiratory medicine clinical services / clinics.

Clinical staff checked the eligibility of patients during their routine hospital consultation (face to face or virtual). If eligible, clinical staff asked the patient for permission to pass their contact details to the research team who provided them with a copy (paper or electronic) of the patient information sheet (PIS). The research team contacted the patient after a minimum of 24 hrs to discuss the study and answer any questions regarding the study and PIS. If the patient was happy to take part in the study, a consent form was sent to them in the post. Potential participants received a telephone call approximately 3 days later. During this call, the research team explained the content of the consent form and participant information sheet. They then answered any questions they had about the study. Finally, the researcher asked the participant to verbally consent. Verbal consent was recorded.

Participants were sent a pre-paid return envelope to return the signed and dated copy of their consent form to the research team. Finally, a countersigned copy of the consent form was sent to participants in the post.

**Population**

Patients living with chronic breathlessness due to advanced malignant or non-malignant disease.

**Inclusion criteria**

- Adults ≥ 18 years of age
- Chronic breathlessness (CB) defined as breathlessness that persists despite optimal pharmacological treatment of the underlying lung disease including: chronic obstructive pulmonary disease (COPD), asthma, interstitial lung disease (ILD), chronic fibrotic lung disease following SARS-CoV2 infection, bronchiectasis, cystic fibrosis (CF), and lung cancer
- Modified Medical Research Council (mMRC) dyspnea score ≥ 2 (mMRC = *walks slower than contemporaries on the level due to breathlessness or has to stop when walking at own pace)[28]*
- Access to a computer or tablet or smart phone with internet access
- Able to provide informed consent

**Exclusion criteria**

- Breathlessness of unknown cause
- Primary diagnosis of chronic hyperventilation syndrome
- Currently participating in a rehabilitation programme e.g., pulmonary/cardiac rehabilitation ~~(patients that have completed PR within 4-weeks will be eligible).~~

**Data collection**

Research data was collected simultaneously in both groups. Baseline [(prior to randomisation (T1)] and at 6 weeks post randomisation (T2) using self-complete postal questionnaires.

**Patient demographic and characterisation data**
At baseline, participants were asked to self-complete a demographic questionnaire which included the following: age, sex, ethnicity, educational level, employment status smoking status, MRC dyspnea score, living status (alone vs living with others), self-reported confidence in using the internet measured on a 0 – 10 numerical rating scale (NRS) (0 = no confidence, 10 = extremely confident.

**Feasibility outcomes**

**Primary outcome**
The number of patients recruited into this study over a 12-month period. The recruitment target for this study was 40 patients.

**Secondary outcomes**
- Proportion of patients willing to be randomised
- Proportion of patients remaining in the study at six weeks (primary end point, T2)
- Proportion of, and reasons for, patients with missing data e.g., research questionnaires
- Frequency of SELF-BREATHE logins
- Number of reported technical faults

***A priori*** **progression criteria**
Based on previous interventional studies in chronic breathlessness [11, 12], and clinical services such as pulmonary rehabilitation (PR) the follow progression criteria have been set for this study;
- **30%** of eligible patients given an information sheet consent to participation in the study
- **≥ 60%** of the patients log on and access SELF–BREATHE, within 2 weeks
- **≥ 70%** of patients report the methodology and intervention as acceptable

**Patient Reported Outcomes Measures (PROMs)**
To quantify the affective and effective components of chronic breathlessness the following validated and responsive PROMs were measured at both time points (T1 and T2);

- **Breathlessness severity** at rest, on exertion and worst over the last 24 hours assessed on a 0 – 10 numerical rating scale (NRS) (0 = no shortness of breath, 10 = worse possible)

- **Dyspnea 12** quantifies breathlessness using 12 descriptors that tap into the physical and affective aspects of dyspnea [30]

- **The London Chest Activity of Daily Living Scale (LCADL**) measures the functional impact of breathlessness on activities of daily living e.g., self – care [31]

- **Confidence in breathlessness** self-management will be measured using the question; "how confident are you that you can keep your shortness of breath from interfering with what you want to do? Scored on 0 - 10-point scale (0 = not at all confident, 10 = totally confident) [33]

- **Illness perception**: the Brief Illness Perception Questionnaire (Brief IPQ) is a 9-item questionnaire designed to rapidly assess cognitive and emotional representations of illness [35]

- **Acceptability of SELF-BREATHE:** acceptability was assessed via a Likert Scale Questionnaire (range 1-5). Participants were asked to respond to specific questions reflecting the overall acceptability of SELF-BREATHE and potential benefits (table 3) [29]

**Health service use**

Self-reported health service questions captured GP (General Practitioner or family doctor) contacts, planned and unplanned hospital / emergency department attendances, and hospitalisations, the main cost drivers associated with chronic breathlessness.

**Explanatory qualitative interviews**

Participants allocated to the intervention group (SELF-BREATHE) were invited to take part in semi-structured in–depth interviews to understand perceived value of SELF-BREATHE, positive and negative experiences of using an internet-based intervention, and possible refinements / improvements. Interviews were audio-recorded, transcribed verbatim and analysed using conventional content analysis [29]. This approach commences with immersion in the data. After reading each transcript word by word, codes are derived to capture key thoughts and concepts, and subsequently refined and sorted into meaningful categories and clusters. Analysis included deductive coding structured around the interview topic guide, and inductive analysis to extract any other pertinent findings specifically in relation to potential modifications and improvements to the intervention. Coding was led by the principal investigator (CCR), a physiotherapist experienced in qualitative research, and supported by the qualitative lead for the project (KB), a qualitative methodologist, who reviewed the analysis and conducted line-by-line coding on a sample of data extracts. The coding frame and summary findings were reviewed by the extended research team and subsequently refined.

**Sample size**

This study was designed to assess the feasibility of conducting a randomised controlled trial of SELF-BREATHE to determine the optimum method of evaluation, and understand users" experiences and perceived value of SELF-BREATHE, therefore a formal power calculation was not required. Sample sizes between 20 and 50 have been recommended for feasibility

trials [26, 27]. Using a pragmatic approach, a target sample size of 40 patients was set for this study, as it was deemed sufficient to assess feasibility parameters including recruitment rates, trial compliance, willingness to be randomised, and to explore potential primary and secondary outcome measures with standard deviations.

We aimed to conduct qualitative interviews in a purposive sample of 10-12 patients, with recruitment continuing until sufficient information power was achieved to address the qualitative objectives [30]. This was to be determined by preliminary analysis of detailed reflective notes taken immediately after interviews, and constant comparison of new data with existing findings [17]. We anticipated that due to the depth of knowledge and information participants held about their experience of SELF-BREATHE and the trial itself, approximately 10 – 12 participants would be required to provide adequate information power.

**Randomisation and blinding**

Data from the baseline interview was sent by secure e-mail to the King‟s Clinical Trials Unit (CTU). The CTU online randomisation system allocated participants to study arms, independent of the research and clinical teams. Randomisation was done by minimisation [28] to balance three potential confounders between trial arms identified from published data [14]: cancer versus non-cancer, breathlessness severity (NRS >3 or not), and presence (or not) of an informal caregiver.

Following randomisation, the CTU team informed the SELF-BREATHE administrator of each patient‟s study arm via secure e-mail. The administrator contacted participants to inform them of their allocated study arm. For participants allocated to SELF-BREATHE they were contacted by phone, email and letter providing them with their website username, temporary password, user guide and „go live“ date. This was followed up with a telephone call by the administrator, to ensure that the participant had been able to access SELF-BREATHE. The research assistant entering the data to the database was blind to trial arm allocation.

**Intervention arm: SELF-BREATHE**

SELF-BREATHE is a complex, transdiagnostic, breathlessness, supportive digital intervention co-developed with patients following the IDEAS and MRC frameworks [19, 23] , theoretically underpinned by Leventhal‟s Common-Sense Model of Self-Regulation [24-26].

Participants allocated to the intervention group (SELF-BREATHE) continued to receive their usual NHS care, but they were also given a username and password, which provided unlimited access to SELF-BREATHE throughout the study duration.

SELF-BREATHE has seven core components, delivered via multi model media (i.e., animations, written text, audio files, pictures, and instructional videos).

1. **Patient education** about chronic breathlessness and self-management

2. **Patient self-monitoring of their breathlessness**: breathlessness severity, distress due to breathlessness, impact of breathlessness on daily life, with real-time algorithm based automated feedback
3. **Breathing exercises and techniques:** methods to improve breathlessness self-management e.g., breathing control exercises, purse lipped breathing, body positions to relieve breathlessness
4. **Breathlessness self-management planning:** patients can formulate a personalised breathlessness crisis plan, which will include the breathlessness management techniques used at points of breathlessness crisis e.g., breathing control
5. **Improving physical activity:** advice on how to increase daily activity levels, self-directed and self- monitored home exercise programme of bed, chair and standing based exercises
6. **Personalised Goal Setting:** self-guided support for patients to set personalised goals and how to track achievement and success
7. **Ask the expert:** inbuilt messaging service where patients can ask a question or get advice about any specific aspect of SELF-BREATHE (responses were provided by CCR, Consultant Physiotherapist, within 48 hours)

Behaviour change techniques were identified from the development phase of SELF-BREATHE which was conducted with patients [23]. The techniques identified include: (i) information about health consequences, (ii) self-monitoring, (iii) demonstration and instruction of breathing techniques and home exercise programmes, (iv) breathing technique practice and rehearsal sessions, (v) goal setting, and (vi) action planning [31].

Participants were advised to log in to SELF-BREATHE within 72 hrs of receiving their login details, and over the six-week period work through the seven component sections in a stepwise fashion, personalising and implementing suggested interventions e.g., breathing control exercises, home exercise etc. Establishment of these self-management techniques within participants‟ day-to-day lives was supported through optional interactive components of SELF-BREATHE e.g., self-monitoring of their progress including self-reporting of their breathlessness severity, goal setting, and attainment.

Participants were provided with a telephone number and email address where they could access help and support with any technical problems. Once participants had received their login details, they did not have any planned contact with the research team or health profession until the 6-week follow up time point. SELF-BREATHE has an “ask the expert” function that participants could use.

SELF-BREATHE was hosted by UKFAST, a Tier III data centre with ISO27001 Certification, IG Toolkit Level 2, in compliance with NHS data governance policy.

**Control arm: usual NHS care**

Patients randomised to the control group continued with their usual NHS care, as was available to them prior to entry into the trial. There are no widely used, NHS commissioned

breathlessness support services, therefore the comparator was usual care.

Usual care: all patients were registered with an NHS GP (General practitioner or family doctor) and had access to them as needed. All patients were under the care of a Consultant Respiratory Physician, reviewing patients at regular intervals, usually every 6-12 months. All patients had access to NHS Accident and Emergency Departments, where patients could attend by calling an emergency ambulance or by visiting the emergency department with their own transport. Emergency and planned hospital admission was available to all.

**Patient and public involvement**

Patient and public involvement (PPI) was imbedded within the initial project proposal and throughout the study. Six PPI representatives from the Cicely Saunders Institute PPI group, King‟s College London (https://www.csipublicinvolvement.co.uk), participated in different aspect of SELF-BREATHE development and trial processes, including: providing feedback on SELF-BREATHE prototypes, SELF-BREATHE content development, development of study related materials such as participant information sheets, and attending trial steering group and management meetings.

**Analysis**

Simple descriptive statistics were used to summarise the number of patients referred, approached, consented, and randomised (total and split by primary diagnosis), plus summarised in line with the CONSORT statement [36]. Proportions of participants that i) logged in and used SELF-BREATHE and ii) remained in the study at six weeks (T2) were reported. In keeping with the feasibility design, baseline characteristics and clinical outcome data have been summarised descriptively with no formal statistical testing for superiority of SELF-BREATHE compared to usual care. Data were analysed and summarised in line with the *a priori* progression criteria.

**Results**

Between 18/01/2021 and 12/01/2022, 110 eligible patients were referred into the study and provided with a participant information sheet. 52 /110 (47%) consented and were randomised into the trial (figure 1), exceeding our recruitment target.

Participants had severe chronic breathlessness due to advanced respiratory disease. Participants were confident internet users with the majority living in areas of high deprivation. Participants reported low self-confidence in their ability to manage their breathlessness (table 1). Within our sample the mean (sd) age was 63 (13) years, of which 31% > 71 years of age, MRC dyspnea score 2.4 (1), of which 40.5% had an MRC > 4, demonstrating that patients across a wide range of ages and disease severity were recruited.

Of participants randomised to SELF-BREATHE, 19 of the 26 (73%) logged in and used SELF-BREATHE. Individuals logged into SELF-BREATHE mean (standard deviation, range) 9 (8, 1-33) times over 6-weeks. Thirty six of the 52 randomised participants (70%)

completed and returned the end of study postal questionnaires at week six (figure 1). Missing data was greatest in the intervention arm (SELF-BREATHE) (figure 1). Those that did not complete the end of the study postal questionnaires tended to be older and had more severe breathlessness related disability (higher MRC scores) (table 1).

Reason for missing data: two participants completed end of study postal questionnaires, but these were not received by the research team, two participants withdrew from the study after randomisation to the control arm, and study questionnaires for 12 participants were not returned (reasons unknown).

End of study patient reported outcomes measured at 6 weeks are summarised in table 2. All participants pre–randomisation reported that the study design was acceptable. Two of the 26 (7.7%) participants allocated to the control arm reported that they were "*disappointed*" to have been allocated to this arm but were happy to continue their participation in the trial. SELF-BREATHE users reported it to be acceptable (table 3). SELF-BREATHE users reported that it improved both their understanding of chronic breathlessness and breathlessness self-management (table 3).

Post intervention qualitative interviews demonstrated that SELF-BREATHE was acceptable and valued, by users, and provided interventions that they perceived to improve their breathlessness.

> *"My main goal [as part of SELF-BREATHE] was to go walking because I really enjoyed walking. Since I'd had COVID, that all came to a stop. I was battling [with breathlessness] to get to the front door. So, I've managed to get out. Obviously, at the beginning somebody had to be with me. But now, I've actually ventured out on my own with the dog."* **Female, Asthma, 61-70 years.**

> *"SELF-BREATHE is very directed at self-motivation, so I did it every other day or every day sometimes. One thing that I found very, very useful was the idea of using the fan when you're breathless, that really worked for me, so I do that constantly all the time now. The exercises were really good and some of them I am continuing to do. I would say it's [SELF-BREATHE] helped me control my breathing".* **Male, ILD, 51-60 years.**

Participants also described the positive impact of SELF-BREATHE on both their physical and mental health:

> *"I was sceptical I have to be honest, but after a week or so I started to see the benefits of how to control my breathing when moving around and walking, it [SELF-BREATHE] also encouraged me to set my own goals, one being to walk more steps in*

*a day, I'm now above 5,000 steps a day. It takes commitment from you to take part but is so very worth it. I know I can't be cured but it has certainly helped me in controlling my breathing and also my mental health.*" **Male, ILD, 51-60 years.**

In addition, SELF-BREATHE was found to be helpful at point of breathlessness crisis:

"*It was good [SELF-BREATHE} because obviously when you have a breathing attack you automatically just clam up and panic. But it was nice to be able to have that information to hand [SELF-BREATHE}."*

*"*What did you find useful when you had these breathlessness attacks?"

*"The [breathing] techniques and everything, especially with the pursed lips, the relaxation. The bending over and breathing from the diaphragm that helped."*
**Female, COPD, 41-50 years.**

One participant struggled to use SELF-BREATHE due to macular degeneration, highlighting that digital / online interventions may needs additional consideration to increase accessibility:

*"I couldn't do much of it [SELF-BREATHE] because of my eyesight, I have macular degeneration. My son came and helped me, but it's just my sight, my eyes are a bit wobbly. Things start running together, the lines, and I find it quite difficult. I think I got to number three or stage three or something and I said to him, "No this is it." I had to give up. Unless you've got it yourself it's hard to understand*". **Female, COPD, 81-90 years.**

**Figure 1:** CONSORT flow diagram

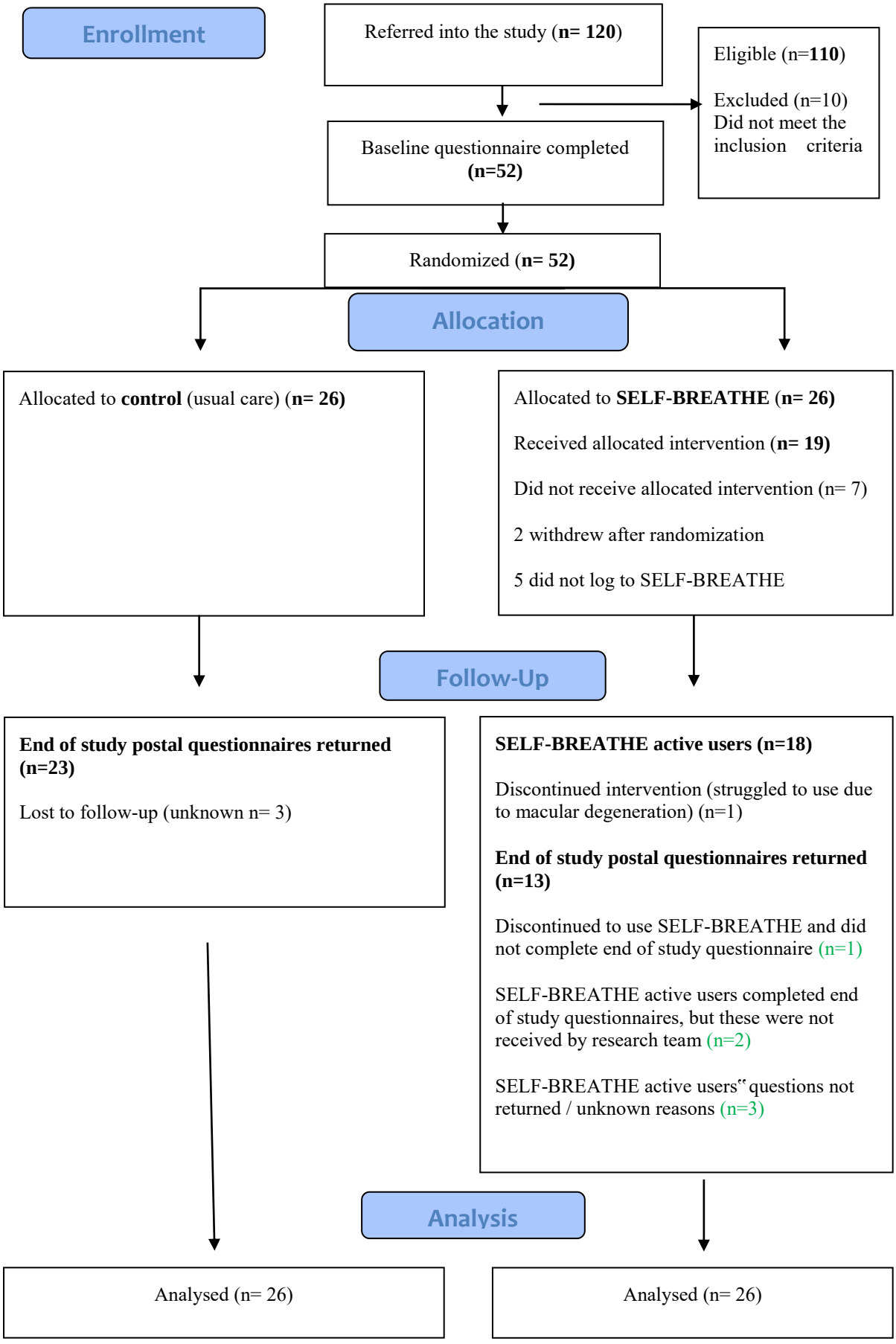

**Table 1:** Baseline demographics and characteristics of all participants that consented and randomised into the feasibility randomised controlled trial of SELF-BREATHE.

| | **All** (n=52) | **Control** (n=26) | **SELF-BREATHE** (n=26) | **Lost to follow up** (n=16) |
|---|---|---|---|---|
| **Age** (years)* | 63 (13) | 63 (13) | 63 (14) | 65 (13.7) |
| **Age Category** | | | | |
| <40 | 3 (5.8%) | 1 (3.8%) | 2 (7.7%) | 1 (6.25%) |
| 41 – 50 | 5 (9.6%) | 2 (7.7%) | 3 (11.5%) | 1 (6.25%) |
| 51 – 60 | 8 (15.4%) | 5 (19.2%) | 3 (11.5%) | 2 (12.5%) |
| 61 – 70 | 20(38.5%) | 10 (38.5% | 10 (38.5%) | 6 (37.5%) |
| 71 – 80 | 12 (23.1%) | 7 (26.9%) | 5 (19.2%) | 3 (18.75%) |
| 81 – 90 | 4 (7.7%) | 1 (3.8%) | 3 (11.5%) | 3 (18.75%) |
| **NRS confidence internet use*** [$] | 7.6 (2.3) | 7.5 (2.2) | 7.7 (2.4) | 7.8 (2.5) |
| **NRS confidence in breathlessness self-management*** [$] | 4.3 (2.7) | 4.1 (2.8) | 4.5 (2.6) | 4.7 (2.6) |
| **MRC Dyspnea Score*** [+] | 2.4 (1) | 2.3 (1) | 2.4 (1.1) | 2.8 (1) |
| **MRC Dyspnea Category** [+] | | | | |
| MRC 2 | 10 (19.2%) | 4 (15.4%) | 6 (23%) | 2 (12.5%) |
| MRC 3 | 21 (40.4%) | 13 (50%) | 8 (30.8%) | 4 (25%) |
| MRC 4 | 13 (25%) | 6 (23%) | 7 (26.9%) | 6 (37.5%) |
| MRC 5 | 8 (15.5%) | 3 (11.5%) | 5 (19.2%) | 4 (25%) |
| **Sex** (Male: Female) | 31:21 | 15: 11 | 16: 10 | 9:7 |
| **Ethnicity** [#] | | | | |
| *White* | 42 (80.8%) | 20 (76.9%) | 22 (84.6%) | 14 (87.5%) |
| *Asian or Asian British* | 4 (7.7%) | 4 (15.4%) | | 1 (6.3%) |
| *Black, African, Caribbean or Black British* | 1 (1.9%) | - | 1 (3.8%) | 1 (6.3%) |
| *Mixed* | 2(3.8%) | - | 2 (7.7%) | - |
| *Other* | 3 (5.8%) | 2(7.7%) | 1 (3.8%) | - |
| **Primary Diagnosis** | | | | |
| COPD | 31 (59.6%) | 19 (73%) | 12(46.2%) | 11 (68.8%) |
| Interstitial Lung Disease (ILD) | 5 (9.6%) | 3 (11.5%) | 2 (7.7%) | 1 (6.3%) |
| Bronchiectasis | 9 (17.3%) | 3 (11.5%) | 6 (23.1%) | -- |
| Cancer | 2(3.8%) | - | 2 (7.7%) | 2 (12.5%) |
| Asthma | 1 (1.9%) | - | 1(3.8%) | - |
| Cystic fibrosis | 1(1.9%) | 1(3.8%) | - | - |
| Long COVID | 3 (5.8%) | - | 3 (11.5%) | 2 (12.5%) |
| **Smoking Status** | | | | |
| *Never* | 13 (25%) | 9 (34%) | 4 (15.4%) | 3 (18.8%) |
| *Ex – smoker* | 36 (69.2%) | 16 (61.5%) | 20 (76.9%) | 11 (68.8%) |
| *Current – smoker* | 3 (5.8%) | 1 (3.8%) | 2 (7.7%) | 2 (12.5%) |
| **Living situation** | | | | |
| *Alone* | 25 (48.1%) | 11(42.4%) | 14 (53.8%) | 6 (37.5%) |
| *Living with significant other / family* | 27 (51.9%) | 15 (57.7%) | 12 (46.2%) | 10 (62.5%) |
| **Support provided by a carer** | | | | |

| | | | | |
|---|---|---|---|---|
| *Yes* | 29 (55.8%) | 14 (53.8%) | 15 (57.7%) | 10 (62.5%) |
| *No* | 23 (44.2%) | 12 (46.2%) | 11 (42.3%) | 6 (37.5%) |
| **Level of Education** | | | | |
| Left school aged 15 or younger | 11 (21%) | 5 (19%) | 6 (23.1%) | 6 (37.5%) |
| Left school aged 16 -17 | 13 (25%) | 7 (26.9%) | 6 (23.1%) | 4 (25%) |
| Left school aged 18-19 | 2 (3.8%) | - | 2 (7.7%) | 1 (6.3%) |
| Post-secondary school qualification | 8 (15.4%) | 3 (11.5%) | 5 (19.2%) | - |
| University qualification | 18 (34.6%) | 11 (42.3%) | 7 (26.9%) | 5 (31.3%) |
| **Index of multiple deprivation (IMD)** *+ | 23.8 (11.9) | 23 (11.9) | 24.5 (12.1) | 23.3 (11.6) |
| IMD quintile 1 (least deprived) | 5 (9.5%) | 3 (11.5%) | 2 (7.7%) | 2 (12.5%) |
| IMD quintile 2 | 6 (11.5%) | 3 (11.5%) | 3 (11.15%) | 1 (6.3%) |
| IMD quintile 3 | 9 (17.3%) | 3 (11.5%) | 6 (23.1%) | 4 (25%) |
| IMD quintile 4 | 19 (36.5%) | 8 (30.8%) | 11 (42.3%) | 6 (37.5%) |
| IMD quintile 5 (most deprived) | 9 (17.3) | 6 (23.1%) | 3 (11.15%) | 3 (18.75%) |
| **Breathlessness severity** | | | | |
| NRS breathlessness at rest*+ | 5.0 (2.3) | 5.2 (2.5) | 4.8 (2.2) | 4.9 (2.4) |
| NRS breathlessness on exertion*+ | 8.0 (1.7) | 8.6 (1.3) | 7.3 (1.8) | 7.7 (1.8) |
| NRS worst breathlessness in last 24 hours*+ | 6.7 (2.3) | 7.5 (2.1) | 6.2 (2.4) | 6.9 (1.7) |
| Dyspnea 12 total score*+ | 18.4 (8.8) | 19.0 (7.9) | 18.0(9.7) | 19.9 (8.7) |
| Dyspnea 12 physical component*+ | 11.9 (5.1) | 12.7 (4.9) | 11 (5.3) | 12.1 (4.5) |
| Dyspnea 12 emotional component*+ | 6.3 (4.5) | 6.0 (4.1) | 6.6 (4.8) | 7.3 (4.7) |
| **Impact of breathlessness on activities of daily living** | | | | |
| London Chest Activities of Daily Living Questionnaire (LCADL) total score*+ | 37.6 (11.7) | 39.2 (11.3) | 36.2 (12) | 40 (11.9) |
| LCADL - self-care*+ | 12.1 (4.9) | 12.5 (5.1) | 11.6 (4.9) | 12.4 (5.7) |
| LCADL – domestic*+ | 16.1 (8.0) | 16.7 (8.3) | 15.6 (7.9) | 18.1 (7.9) |
| LCADL - physical*+ | 6.0 (1.7) | 5.9 (1.6) | 6.2(1.8) | 6.5 (1.8) |
| LCADL - Leisure*+ | 6.8 (2.4) | 6.7(2.2) | 7.0 (2.6) | 7.0 (2.9) |
| **Illness perception** | | | | |
| The brief illness perception questionnaire*+ | 55.6 (10.8) | 56.7 (8.3) | 54.4 (13.0) | 59.0 (13.0) |

NRS = numerical rating scale 0 -10, MRC Dyspnea = functional disability due to breathlessness, *****= Data reported as mean (standard deviation), **+** = higher score worse, [# =] self-reported, [$] = higher score better

**Table 2**: Summary of patient reported outcomes measured at six weeks, by trial group.

| | **Control (n=23)** Mean (sd) | **SELF-BREATHE (n=13)** Mean (sd) | **Mean difference between groups (95%CI)** |
|---|---|---|---|
| **Breathlessness severity** | | | |
| NRS breathlessness at rest+ | 4.8 (2.7) | 4.6 (2.6) | 0.20 (-1.68 to 2.10) |
| NRS breathlessness on exertion+ | 7.9 (1.5) | 7.1 (2.1) | 0.80 (-0.40 to 1.98) |
| NRS Breathlessness worst+ | 7.4 (1.5) | 6.8 (2.3) | 0.60 (-0.69 to1.93) |
| Dyspnea-12+ | 17.5 (7.9) | 16.7 (9.9) | 0.80 ( -5.73 to 7.35) |
| Dyspnea 12 physical component+ | 11.5 (4.2) | 10.3 (5.6) | 1.20 (-0.90 to 3.31) |
| Dyspnea 12 emotional component+ | 6.3 (5.1) | 6.4 (4.9) | -0.10 (-3.69 to 3.62) |
| **Impact of breathlessness on activities of daily living** | | | |
| London Chest Activity of living Questionnaire (LCADL) + | 38.1 (13.7) | 33.0 (16.7) | 5.10 (-6.80 to 17.01) |
| LCADL self-care+ | 9.3 (3.3) | 7.8 (3.6) | 1.50 (-1.06 to 3.97) |
| LCADL – domestic+ | 16.5 (8.1) | 15.1 (9.5) | 1.30 (-5.37 to 7.91) |
| LCADL - physical+ | 6.3 (1.9) | 5.4 (1.9) | 0.90 (-0.52 to 2.30) |
| LCADL - Leisure+ | 6.9 (2.3) | 5.7 (3) | 1.20 (-0.70 t0 3.11) |
| **Illness perception** | | | |
| The brief illness perception questionnaire+ | 56.4 (8.6) | 53.7 (10.3) | 2.70 (-4.03 to 9.40) |
| **Breathlessness self-management** | | | |
| NRS confidence on breathlessness self-management * | 4.4 (2.5) | 4.8 (2.3) | -0.40 (-2.10 to 1.35) |
| **Self-reported breathlessness specific health care use over the last 6 weeks** | Absolute number | Absolute number | |
| Emergency Department attendance | 1 | 0 | - |
| Hospitalisation | 1 | 0 | - |
| GP attendances | 7 | 3 | - |
| +higher score worse, *higher score better | | | |

**Table 3:** Participant reported acceptability and benefits of SELF-BREATHE (n=13)

| Question | Median (IQR) | Range (min – max) |
|---|---|---|
| **How acceptable was it to use SELF-BREATHE?**<br>(1=completely unacceptable, 5= completely acceptable) | 4 (4 -4.5) | 4-5 |
| **How acceptable was the content of SELF-BREATHE?**<br>(1=completely unacceptable, 5= completely acceptable) | 4 (4-5) | 4-5 |
| **How easy was it to understand the content within SELF-BREATHE?**<br>(1 = very difficult, 5 = very easy) | 4 (4-5) | 3-5 |
| **How effective was SELF-BREATHE at improving your understanding about chronic breathlessness?**<br>(1= very ineffective, 5 = very effective) | 4 (4-4) | 3-4 |
| **How effective was SELF-BREATHE at improving your breathlessness self-management?**<br>(1= very ineffective, 5 = very effective) | 3.5 (3-4) | 3-4 |

## Discussion

### Key findings

This is the first feasibility, randomised controlled trial of an online, transdiagnostic, self-management, breathlessness, supportive intervention (SELF-BREATHE) for individuals living with chronic breathlessness due to advanced disease. In line with our research objectives and *a priori* progression criteria we found that an efficacy RCT trial of SELF-BREATHE using our methodology and procedures is likely to be feasible and acceptable to participants.

The feasibility of an efficacy RCT of SELF-BREATHE is supported by the completion of trial procedures, all patients who completed baseline measures were randomised (n =52). Of the 52 participants randomised 36 (70%) completed postal questionnaires which were received by the research team. A systematic review and meta-analysis of palliative care trials (n=119) found an overall attrition rate of 29% (95%CI 28 to 30%), in 50.8% (26.5) of cases, attrition was at random, and the most predominate reason was the patient being no longer contactable [32], which was in keeping with our findings.

Patient reported outcomes may suggest benefit with regard to breathlessness severity, impact of breathlessness on activities of daily living and health care utilisation, in this under powered study. These data provide testable hypotheses and evidence to support conducting a fully powered randomised controlled trial of SELF-BREATHE.

SELF-BREATHE was acceptable and valued by users, who reported observed benefits of using SELF-BREATHE during daily life and at the point of breathlessness crisis. This was despite, the complexity and challenges of conducting this RCT during the COVID-19 pandemic. We also propose minor modifications (i.e., multiple methods for data collection face to face, telephone, online and via post to minimise missing data).

### Relevance of findings

High health care costs are associated with chronic breathlessness, influenced by frequent GP and Emergency Department (ED) attendances due to breathlessness crisis [9, 11]. Therefore, it is imperative to find evidence-based cost-effective new approaches. SELF-BREATHE could potentially improve patient reported outcomes, in particular reducing breathlessness severity while preventing the need for emergency hospital attendance. However, a full scale RCT would be needed to test this. This study provides both testable hypotheses and evidence to support an efficacy RCT of SELF-BREATHE.

The COVID-19 pandemic has increased the acceptability, use, normalisation and value of the internet for many patients living with chronic breathlessness due to advanced respiratory disease [23]. The changes in clinical service provision because of the COVID-19, has increased patients‟ willingness to use online self-management interventions such as SELF-BREATHE, a key influencing factor in the success of this study. SELF-BREATHE was

valued by users as it provided them with interventions to improve their breathlessness during daily life and at the point of breathlessness crisis. SELF-BREATHE was co-developed with patients [19, 23] underpinning it acceptability.

A reflection from conducting a trial in patients with chronic breathlessness and advanced disease during a pandemic, is the importance of selecting a primary and secondary outcome measure that can be easily modifiable and valid to collect via different modalities. Having the option for face to face, telephone, virtual and postal completion of measures would be very useful in times of crisis or when research support or resource is low.

**Strengths and limitations**

There are some limitations to this feasibility study. The participants were not blind to group allocation and would have known that they were allocated to the intervention group rather than usual care, which is common in complex behavioural interventions [14, 20]. The researcher entering the research data to the database were blind to group allocation.

Both male and females were well represented in our trial. However, our sample was predominantly white. Under representation of minority ethnic groups in medical research is an ongoing issue in the UK and beyond [20, 33]. Ensuring equity, inclusion and diversity must be a key priority going forward in planning subsequent trials of SELF-BREATHE. Widening participation and geographical reach of PPI members supporting the onward development of SELF-BREATHE, may help engage those from minority ethnic groups. It is also important that a future RCT of SELF-BREATHE is multi centred and inclusive of varied geographical and socio-economic diverse backgrounds, including translation and dubbing of materials as appropriate.

We endeavoured to recruit participants across a broad demographic range, however the reach of our research and SELF-BREATHE can be improved. A consequence of the COVID-19 pandemic is increased digital literacy nationally and internationally [18]. Care must be taken to ensure that digital transformation of services do not amplify healthcare care inequality by facilitating a digital divide, that fails to provide adequate health and social care to those that do not have the skills to benefit [20]. Our data highlighted that for some individuals complex multimorbidity and disability can make engaging with digital healthcare challenging. Therefore, it is important to consider SELF-BREATHE as a potential treatment option for those who are willing and able to engage with self-management and digital innovation.

It is a strength that this study was able to be conducted successfully during the COVID-19 pandemic, but it did increase missing data. Some missing data can be directly accounted for due to extrinsic factors e.g., two questionnaires completed in the intervention arm were posted but were never received by the research team. This is both a limitation of the study design and reflective of the impact COVID-19 had on the infrastructure, including postal services. This study highlights important methodological considerations from conducting a

RCT during a pandemic (i.e., the importance of multi- methods approach to data capture to minimise missing data).

For 12 of the 16 participants for whom we did not receive the end of study questionnaires, we do not have a known reason for this missing data. Those that were lost to follow up tended to be older with higher breathlessness related disability. One could hypothesise that for these older individuals with more severe disease, having to physically return the end of study postal questionnaires may have been too challenging for them. Support networks were reduced or became non-existent during the pandemic, due to the government enforced restrictions, and due to COVID-19 infection. Thus, for our participants, retuning a postal question may have been impractical, or a low priority for them.

Another influencing factor with regard to the level of missing data is the lack of research support resources available during the COVID-19 pandemic. Indeed, the PI (CR) and research nurses were redeployed to support the acute COVID-19 wards. In addition, high sickness rates across the clinical–academic workforce resulted in lack of resources to consistently follow up on un-returned questionnaires. The pre-COVID study protocol was to conduct all baseline and follow up research questionnaires within the participant‟s own home. This approach has been shown to be advantageous in minimising missing data in patients with advanced disease, and to help engage those that are housebound and unable to attend hospital research visits [14, 34]. Our data provides new and valuable insights in terms of the methodological challenges of conducting a clinic trial during a global pandemic. In comparison to face to face home visits, postal questionnaires can be cost and resource efficient. In hindsight collecting follow-up data over the telephone or via online video call may have helped minimise missing data.

## Conclusion

A randomised controlled trial of SELF-BREATHE was feasible to conduct. SELF-BREATHE was acceptable to individuals living with chronic breathlessness due to advanced disease. These data support the feasibility and acceptability of an efficacy RCT of SELF-BREATHE, with modifications to minimise missing data (i.e., multiple methods for data collection, face to face, telephone, video assessment and via post).

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**Figure 1:** CONSORT flow diagram