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

Charles C. Reilly [1,2], Matthew Maddocks[2], Trudie Chalder[3], Katherine Bristowe[2] and Irene J. Higginson [2]

[1]Department of Physiotherapy, King's College Hospital, London, UK. [2]Cicely Saunders Institute of Palliative Care, Policy and Rehabilitation, King's College London, London, UK. [3]King's College London, Institute of Psychiatry, Department of Psychological Medicine, London, UK.

Corresponding author: Charles Reilly (charles.c.reilly@kcl.ac.uk)

Shareable abstract (@ERSpublications)
SELF-BREATHE is acceptable and valued by users. These data support the feasibility of moving to a fully powered, randomised controlled trial of SELF-BREATHE with minor modifications, *i.e.* multiple methods for data collection to minimise missing data. https://bit.ly/3WCRo3s

Cite this article as: Reilly CC, Maddocks M, Chalder T, *et al*. A randomised, controlled, feasibility trial of an online, self-guided breathlessness supportive intervention (SELF-BREATHE) for individuals with chronic breathlessness due to advanced disease. *ERJ Open Res* 2023; 9: 00508-2022 [DOI: 10.1183/23120541.00508-2022].

Received: 30 Sept 2022
Accepted: 17 Dec 2022

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 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 National Health Service (NHS) care). The setting was a large multisite NHS foundation trust in south-east London, UK. The participants were patients living with chronic breathlessness due to advanced malignant or nonmalignant disease(s). Participants were randomly allocated (1:1) to an online, self-guided, breathlessness supportive intervention (SELF-BREATHE) and usual care or usual care alone, over 6 weeks. The *a priori* progression criteria were ⩾30% of eligible patients given an information sheet consented to participate; ⩾60% of participants logged on and accessed SELF-BREATHE within 2 weeks; and ⩾70% of patients reported the methodology and intervention as acceptable.

Results Between January 2021 and January 2022, 52 (47%) out of 110 eligible patients consented and were randomised. Of those randomised to SELF-BREATHE, 19 (73%) out of 26 logged on and used SELF-BREATHE for a mean±SD (range) 9±8 (1–33) times over 6 weeks. 36 (70%) of the 52 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, randomised controlled efficacy trial with minor modifications to minimise missing data (*i.e.* multiple methods of data collection: face-to-face, telephone, video assessment and by post).

Introduction

Worldwide, >75 million people have breathlessness, including >90% of the 65 million people with severe lung disease [1], >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 multimorbidities [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 coronavirus disease 2019 (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 healthcare 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 attendance and hospitalisations [10–12].

There is good evidence for breathlessness supportive services delivered face-to-face, which focus on education and nonpharmacological approaches to chronic breathlessness self-management [13, 14]. Breathlessness supportive service 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 ⩾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 suggest that internet use, and in particular the use of video communication applications, have increased exponentially during the COVID-19 pandemic [16]. An increase in internet access and digital literacy in people with chronic respiratory disease has been observed in the UK during the COVID-19 pandemic [18]. Those living with chronic breathlessness due to advanced disease and who have 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, pre-pandemic, others had reported challenges with recruiting, retaining and engaging patients [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, supportive breathlessness digital intervention co-developed with patients following the Integrate, Design, Assess and Share (IDEAS) and Medical Research Council (MRC) 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 nonpharmacological self-management approaches [19, 23].

The aim of this study was primarily to determine whether a randomised controlled trial (RCT) 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 who 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], the evaluating complex interventions in end of life care (MORECare) statement [27], the Consolidated Standards of Reporting Trials (CONSORT) statement (www.consort-statement.org) 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/Health Research Authority 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 RCT 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 NHS Foundation Trust (Denmark Hill and Princess Royal University Hospital sites) where there is high prevalence of chronic breathlessness, *e.g.* integrated respiratory teams, 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. The research team contacted the patient after a minimum of 24 h to discuss the study and answer any questions regarding the study and patient information sheet. 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 ∼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 participants had about the study. Finally, the researcher asked the participant to consent verbally. 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 nonmalignant disease.

Inclusion criteria

- Adults aged ⩾18 years.
- Chronic breathlessness defined as breathlessness that persists despite optimal pharmacological treatment of the underlying lung disease, including COPD, asthma, interstitial lung disease (ILD), chronic fibrotic lung disease following severe acute respiratory syndrome coronavirus 2 infection, bronchiectasis, cystic fibrosis and lung cancer.
- MRC dyspnoea score ⩾2 (short of breath when hurrying on the level or walking up a slight hill) [28].
- Access to a computer or tablet or smartphone 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.

Data collection

Research data were collected simultaneously in both groups: at baseline (prior to randomisation (T1)) and at 6 weeks post-randomisation (T2) using self-completed postal questionnaires.

Patient demographic and characterisation data

At baseline, participants were asked to self-complete a demographic questionnaire which included age, sex, ethnicity, educational level, employment status, smoking status, MRC dyspnoea score, living status (living

alone *versus* living with others) and 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 6 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, the following 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 outcome measures

To quantify the affective and effective components of chronic breathlessness, the following validated and responsive patient-reported outcome measures were measured at both time points (T1 and T2).

- Breathlessness severity at rest, on exertion and worst over the past 24 h assessed on a 0–10 NRS (0=no shortness of breath, 10=worst possible shortness of breath).
- Dyspnea-12, which quantifies breathlessness using 12 descriptors that tap into the physical and affective aspects of dyspnoea [29].
- The London Chest Activity of Daily Living scale measures the functional impact of breathlessness on activities of daily living, *e.g.* self-care [30].
- Confidence in breathlessness self-management that was 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 a 0–10-point scale (0=not at all confident, 10=totally confident) [31].
- Illness perception was measured using the Brief Illness Perception Questionnaire, a nine-item questionnaire designed to rapidly assess cognitive and emotional representations of illness [32].
- Acceptability of SELF-BREATHE 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 its potential benefits [33].

Health service use

Self-reported health service questions captured general practitioner (GP; 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 the perceived value of SELF-BREATHE; positive and negative experiences of using an internet-based intervention; and possible refinements or improvements. Interviews were audio-recorded, transcribed verbatim and analysed using conventional content analysis [33]. 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 (C.C. Reilly), a physiotherapist experienced in qualitative research, and supported by the qualitative lead for the project (K. Bristowe), 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 RCT 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 and 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 [29]. 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, ∼10–12 participants would be required to provide adequate information power.

Randomisation and blinding

Data from the baseline interview was sent by secure email 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* noncancer, 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 email. 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, supportive digital breathlessness intervention codeveloped 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* multimodal 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 and 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 C.C. Reilly, consultant physiotherapist, within 48 h).

Behaviour-change techniques were identified from the development phase of SELF-BREATHE, which was conducted with patients [23]. The techniques identified include 1) information about health consequences;

2) self-monitoring; 3) demonstration and instruction of breathing techniques and home exercise programmes; 4) breathing technique practice and rehearsal sessions; 5) goal setting; and 6) action planning [30].

Participants were advised to log in to SELF-BREATHE within 72 h of receiving their login details, and over the 6-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 ISO 27001 certification, Information Governance 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.

All patients were registered with an NHS GP 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 using 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 (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), and summarised in line with the CONSORT statement. Proportions of participants who 1) logged in and used SELF-BREATHE and 2) remained in the study at 6 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 January 2021 and 12 January 2022, 110 eligible patients were referred into the study and provided with a participant information sheet. 52 (47%) out of 110 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). The mean±SD age was 63±13 years within our sample, of whom 31% were aged >71 years; MRC dyspnoea score was 2.4±1, of whom 40.5% had an MRC >4; thus demonstrating that patients across a wide range of ages and disease severity were recruited.

Of participants randomised to SELF-BREATHE, 19 (73%) out of the 26 logged in and used SELF-BREATHE. Individuals logged into SELF-BREATHE a mean±SD (range) 9±8 (1–33) times over 6 weeks. 36 (70%) of the 52 randomised participants completed and returned the end-of-study postal

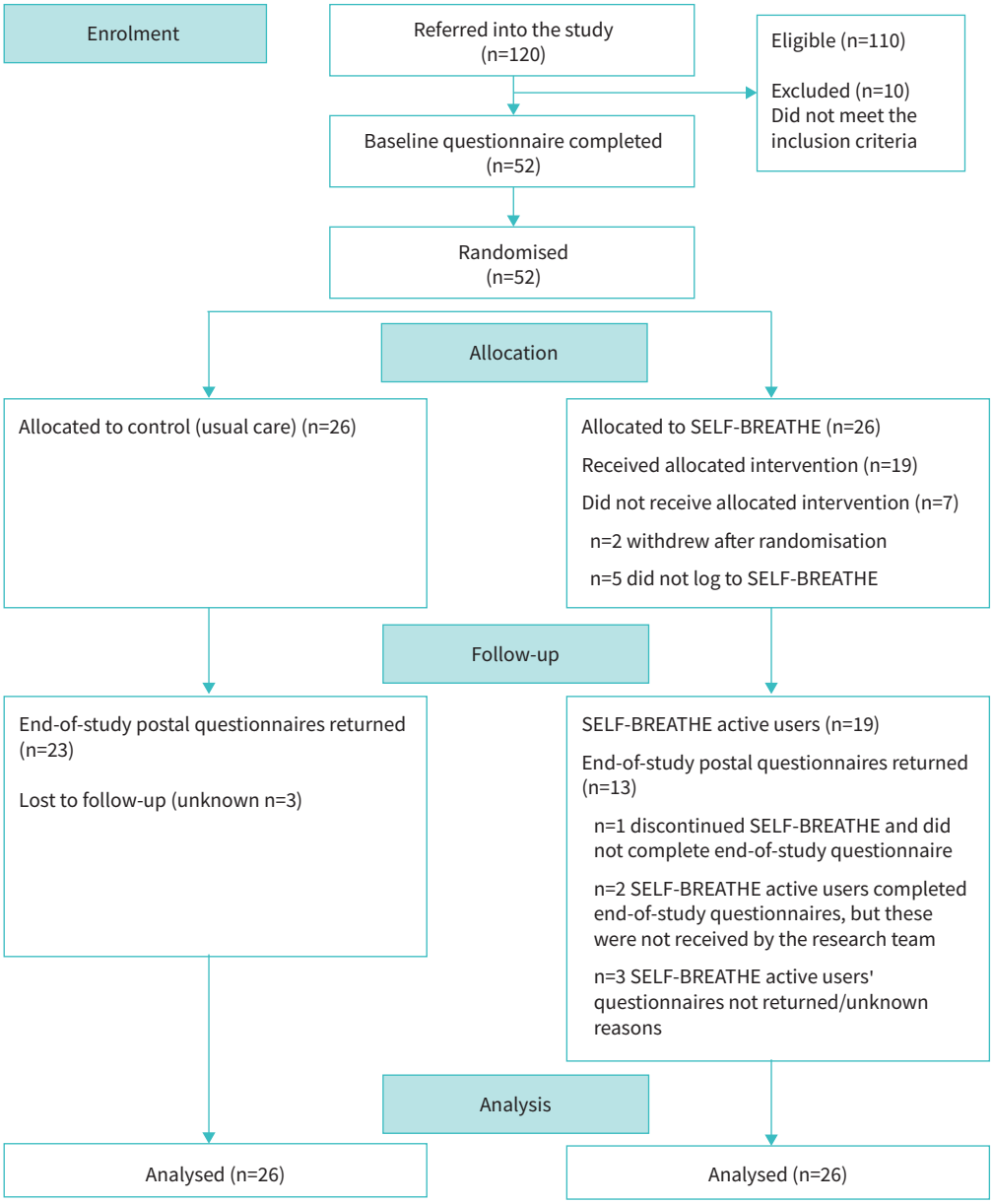

FIGURE 1 Consolidated Standards of Reporting Trials flow diagram.

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

Reasons 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 intervention 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. Pre-randomisation, all participants reported that the study design was acceptable. Two (7.7%) out of the 26 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).

TABLE 1 Baseline demographics and characteristics of all participants who consented and were randomised into the feasibility randomised controlled trial of SELF-BREATHE

	All	Control	SELF-BREATHE	Lost to follow-up
Participants	52	26	26	16
Age years	63±13	63±13	63±14	65±13.7
Age category years				
<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 breathlessness self-management[#]	4.3±2.7	4.1±2.8	4.5±2.6	4.7±2.6
MRC dyspnoea score[¶,+]	2.4±1	2.3±1	2.4±1.1	2.8±1
MRC dyspnoea 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)
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)
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-smoker	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 years	11 (21)	5 (19)	6 (23.1)	6 (37.5)
Left school aged 16–17 years	13 (25)	7 (26.9)	6 (23.1)	4 (25)
Left school aged 18–19 years	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[¶]	23.8±11.9	23±11.9	24.5±12.1	23.3±11.6
Quintile 1 (least deprived)	5 (9.5)	3 (11.5)	2 (7.7)	2 (12.5)
Quintile 2	6 (11.5)	3 (11.5)	3 (11.15)	1 (6.3)
Quintile 3	9 (17.3)	3 (11.5)	6 (23.1)	4 (25)
Quintile 4	19 (36.5)	8 (30.8)	11 (42.3)	6 (37.5)
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 past 24 h[¶]	6.7±2.3	7.5±2.1	6.2±2.4	6.9±1.7

Continued

TABLE 1 Continued

	All	Control	SELF-BREATHE	Lost to follow-up
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				
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				
Brief Illness Perception Questionnaire[¶]	55.6±10.8	56.7±8.3	54.4±13.0	59.0±13.0

Data are presented as n, mean±SD or n (%). NRS: numerical rating scale (0–10); MRC: Medical Research Council; ILD: interstitial lung disease; COVID: coronavirus disease; LCADL: London Chest Activities of Daily Living questionnaire. [#]: higher score better; [¶]: higher score worse; [+]: functional disability due to breathlessness; [§]: self-reported.

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*

TABLE 2 Summary of patient-reported outcomes measured at 6 weeks, by trial group

	Control	SELF-BREATHE	Mean difference between groups (95% CI)
Participants	23	13	
Breathlessness severity			
NRS breathlessness at rest[#]	4.8±2.7	4.6±2.6	0.20 (−1.68–2.10)
NRS breathlessness on exertion[#]	7.9±1.5	7.1±2.1	0.80 (−0.40–1.98)
NRS breathlessness worst[#]	7.4±1.5	6.8±2.3	0.60 (−0.69–1.93)
Dyspnea-12[#]	17.5±7.9	16.7±9.9	0.80 (−5.73–7.35)
Dyspnea-12 physical component[#]	11.5±4.2	10.3±5.6	1.20 (−0.90–3.31)
Dyspnea-12 emotional component[#]	6.3±5.1	6.4±4.9	−0.10 (−3.69–3.62)
Impact of breathlessness on activities of daily living			
LCADL[#]	38.1±13.7	33.0±16.7	5.10 (−6.80–17.01)
LCADL self-care[#]	9.3±3.3	7.8±3.6	1.50 (−1.06–3.97)
LCADL domestic[#]	16.5±8.1	15.1±9.5	1.30 (−5.37–7.91)
LCADL physical[#]	6.3±1.9	5.4±1.9	0.90 (−0.52–2.30)
LCADL leisure[#]	6.9±2.3	5.7±3	1.20 (−0.70–3.11)
Illness perception			
Brief Illness Perception Questionnaire[#]	56.4±8.6	53.7±10.3	2.70 (−4.03–9.40)
Breathlessness self-management			
NRS confidence on breathlessness self-management[¶]	4.4±2.5	4.8±2.3	−0.40 (−2.10–1.35)
Self-reported breathlessness-specific healthcare use over the past 6 weeks			
Emergency department attendance	1	0	
Hospitalisation	1	0	
GP attendances	7	3	

Data are presented as n or mean±SD, unless otherwise stated. NRS: numerical rating scale (0–10); LCADL: London Chest Activities of Daily Living questionnaire; GP: general practitioner. [#]: higher score worse; [¶]: higher score better.

TABLE 3 Participant-reported acceptability and benefits of SELF-BREATHE (n=13)

	Median (interquartile range)	Range (minimum–maximum)
How acceptable was it to use SELF-BREATHE? (1=completely unacceptable, 5=completely acceptable)	4 (4–4.5)	4–5
How acceptable was the content of SELF-BREATHE? (1=completely unacceptable, 5=completely acceptable)	4 (4–5)	4–5
How easy was it to understand the content within SELF-BREATHE? (1=very difficult, 5=very easy)	4 (4–5)	3–5
How effective was SELF-BREATHE at improving your understanding about chronic breathlessness? (1=very ineffective, 5=very effective)	4 (4–4)	3–4
How effective was SELF-BREATHE at improving your breathlessness self-management? (1=very ineffective, 5=very effective)	3.5 (3–4)	3–4

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

In addition, participants 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 5000 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

Furthermore, 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 need 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

Discussion

Key findings

This is the first feasibility RCT 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). Out 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 28–30%); in 50.8±26.5% of cases, attrition was at random, and the most predominant reason was the patient being no longer contactable [34], 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 healthcare utilisation, in this underpowered 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. In addition, we 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 healthcare costs are associated with chronic breathlessness, influenced by frequent GP and emergency department attendances due to breathlessness crises [9, 11]. Therefore, it is imperative to find new evidence-based cost-effective 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 pandemic 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 its 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 resources are 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 was blind to group allocation.

Both males 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 United Kingdom and beyond [20, 31]. 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. In addition, it is important that a future RCT of SELF-BREATHE is multicentred and inclusive of varied geographical and diverse socioeconomic 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 inequality by facilitating a digital divide that fails to provide adequate health and social care to those who 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 could 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 of COVID-19 on infrastructure, including postal services. This study highlights important methodological considerations of conducting a RCT during a pandemic (*i.e.* the importance of a multiple-methods approach to data capture to minimise missing data).

For 12 out 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. Support networks were reduced or became nonexistent during the pandemic, due to government-enforced restrictions, and due to COVID-19 infection. Thus, for our participants, retuning a postal questionnaire may have been impractical, or a low priority.

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 principal investigator (C.C. Reilly) 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 who are housebound and unable to attend hospital research visits [14, 35]. Our data provide 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

Conducting an RCT of SELF-BREATHE was feasible. 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 and *via* post).

Provenance: Submitted article, peer reviewed.

Acknowledgements: We thank all the patients who participated in this research, and everybody who identified and screened patients for this study, especially the respiratory medicine and physiotherapy departments at King's College Hospital (London, UK).

Support statement: A National Institute for Health and Care Research (NIHR) Clinical Lectureship (ICA-CL-2018-04-ST2-001) supports C.C. Reilly. M. Maddocks is supported by an NIHR Career Development Fellowship (CDF-2017-10-009). M. Maddocks and I.J. Higginson are supported by the NIHR Applied Research Collaboration South London (NIHR ARC South London) at King's College Hospital NHS Foundation Trust. I.J. Higginson is an NIHR Senior Investigator Emeritus. This publication presents independent research funded by the NIHR. The views expressed in this publication are those of the author(s) and not necessarily those of the NHS, NIHR or the Dept of Health and Social Care. Funding information for this article has been deposited with the Crossref Funder Registry.

This study is registered at www.clinicaltrials.gov with identifier number NCT04574050. Individual deidentified participant data (including data dictionaries) will not be shared.

Author contributions: C.C. Reilly was the grant award holder (ICA-CL-2018-04-ST2-001) and chief investigator. Conception and design: C.C. Reilly, K. Bristowe, T. Chalder, I.J. Higginson and M. Maddocks. Data acquisition: C.C. Reilly. Data analysis and interpretation was led by C.C. Reilly, K. Bristowe, IJ Higginson and M. Maddocks. All authors contributed to the integration of the interpretation of the data and provided critical revision of the manuscript for important intellectual content. All authors read and approved the final manuscript.

Conflict of interest: C.C. Reilly received support for the present manuscript from the NIHR; and declares funding received from King's Together and Royal Brompton Hospital – King's Health Partnership Transformation, outside

the submitted work. M. Maddocks has received grants or contracts from National Institute for Health Research (NIHR) Career Development Fellowship (CDF-2017–10-009) and NIHR Applied Research Collaboration South London (NIHR ARC South London) at King's College Hospital NHS Foundation Trust, outside the submitted work. T. Chalder receives salary support from the National Institute for Health Research (NIHR) Mental Health Biomedical Research Centre at South London and Maudsley NHS Foundation Trust and King's College London. The views expressed in this article are those of the authors and not necessarily those of the NIHR or the NHS. K. Bristowe has received grants or contracts from the National Institute for Health Research, Medical Research Council, Health Education England, European Commission, and Marie Curie, outside the submitted work. I.J. Higginson has received grants or contracts from the NIHR, UKRI, Cicely Saunders International and Marie Curie, outside the submitted work.

References

1 Sorenson HM. Palliative care for lung disease: start early, stay late. *Lancet Respir Med* 2013; 1: 279–280.
2 Solano JP, Gomes B, Higginson IJ. A comparison of symptom prevalence in far advanced cancer, AIDS, heart disease, chronic obstructive pulmonary disease and renal disease. *J Pain Symptom Manage* 2006; 31: 58–69.
3 Austin J, Williams R, Ross L, *et al.* Randomised controlled trial of cardiac rehabilitation in elderly patients with heart failure. *Eur J Heart Fail* 2005; 7: 411–417.
4 Sandberg J, Ekström M, Börjesson M, *et al.* Underlying contributing conditions to breathlessness among middle-aged individuals in the general population: a cross-sectional study. *BMJ Open Respir Res* 2020; 7: e000643.
5 D'Cruz RF, Waller MD, Perrin F, *et al.* Chest radiography is a poor predictor of respiratory symptoms and functional impairment in survivors of severe COVID-19 pneumonia. *ERJ Open Res* 2021; 7: 00655-2020.
6 Cares-Marambio K, Montenegro-Jiménez Y, Torres-Castro R, *et al.* Prevalence of potential respiratory symptoms in survivors of hospital admission after coronavirus disease 2019 (COVID-19): a systematic review and meta-analysis. *Chron Respir Dis* 2021; 18: 14799731211002240.
7 Rantala HA, Leivo-Korpela S, Lehto JT, *et al.* Dyspnea on exercise is associated with overall symptom burden in patients with chronic respiratory insufficiency. *Palliat Med Rep* 2021; 2: 48–53.
8 Bausewein C, Booth S, Gysels M, *et al.* Understanding breathlessness: cross-sectional comparison of symptom burden and palliative care needs in chronic obstructive pulmonary disease and cancer. *J Palliat Med* 2010; 13: 1109–1118.
9 Dzingina MD, Reilly CC, Bausewein C, *et al.* Variations in the cost of formal and informal health care for patients with advanced chronic disease and refractory breathlessness: a cross-sectional secondary analysis. *Palliat Med* 2017; 31: 369–377.
10 Kelly AM, Keijzers G, Klim S, *et al.* An observational study of dyspnea in emergency departments: the Asia, Australia, and New Zealand Dyspnea in Emergency Departments Study (AANZDEM). *Acad Emerg Med* 2017; 24: 328–336.
11 Hutchinson A, Pickering A, Williams P, *et al.* Breathlessness and presentation to the emergency department: a survey and clinical record review. *BMC Pulm Med* 2017; 17: 53.
12 Currow DC, Chang S, Ekström M, *et al.* Health service utilisation associated with chronic breathlessness: random population sample. *ERJ Open Res* 2021; 7: 00415–2021.
13 Brighton LJ, Miller S, Farquhar M, *et al.* Holistic services for people with advanced disease and chronic breathlessness: a systematic review and meta-analysis. *Thorax* 2019; 74: 270–281.
14 Higginson IJ, Bausewein C, Reilly CC, *et al.* An integrated palliative and respiratory care service for patients with advanced disease and refractory breathlessness: a randomised controlled trial. *Lancet Respir Med* 2014; 2: 979–987.
15 Yi D, Reilly CC, Wei G, *et al.* Optimising breathlessness triggered services for older people with advanced diseases: a multicentre economic study (OPTBreathe). *Thorax* 2022; in press [https://doi.org/10.1136/thoraxjnl-2021-218251].
16 Statista. Global Digital Population as of January 2021. 2021. www.statista.com/statistics/617136/digital-population-worldwide/.
17 Statista. Internet Usage in the United Kingdom (UK) – Statistics and Facts. 2021. www.statista.com/topics/3246/internet-usage-in-the-uk.
18 Polgar O, Patel S, Walsh JA, *et al.* Digital habits of pulmonary rehabilitation service-users following the COVID-19 pandemic. *Chron Respir Dis* 2022; 19: 14799731221075647.
19 Reilly CC, Bristowe K, Roach A, *et al.* "You can do it yourself and you can do it at your convenience": internet accessibility and willingness of people with chronic breathlessness to use an internet-based breathlessness self-management intervention (SELF-BREATHE): during the COVID-19 pandemic. *ERJ Open Res* 2022; 8: 00557-2021.
20 Ainsworth B, Greenwell K, Stuart B, *et al.* Feasibility trial of a digital self-management intervention 'My Breathing Matters' to improve asthma-related quality of life for UK primary care patients with asthma. *BMJ Open* 2019; 9: e032465.

21 North M, Bourne S, Green B, *et al.* A randomised controlled feasibility trial of E-health application supported care *vs* usual care after exacerbation of COPD: the RESCUE trial. *NPJ Digit Med* 2020; 3: 145.

22 Houchen-Wolloff L, Orme M, Barradell A, *et al.* Web-Based Self-Management Program (SPACE for COPD) for individuals hospitalized with an acute exacerbation of chronic obstructive pulmonary disease: nonrandomized feasibility trial of acceptability. *JMIR Mhealth Uhealth* 2021; 9: e21728.

23 Reilly CC, Bristowe K, Roach A, *et al.* "The whole of humanity has lungs, doesn't it, we are not all the same sort of people": patient preferences and choices for an online, self-guided chronic breathlessness supportive intervention (SELF-BREATHE). *ERJ Open Res* 2022; 8: 00093-2022.

24 Mummah SA, Robinson TN, King AC, *et al.* IDEAS (Integrate, Design, Assess, and Share): a framework and toolkit of strategies for the development of more effective digital interventions to change health behavior. *J Med Internet Res* 2016; 18: e317.

25 Skivington K, Matthews L, Simpson SA, *et al.* A new framework for developing and evaluating complex interventions: update of Medical Research Council guidance. *BMJ* 2021; 374: n2061.

26 Leventhal H, Phillips LA, Burns E. The Common-Sense Model of Self-Regulation (CSM): a dynamic framework for understanding illness self-management. *J Behav Med* 2016; 39: 935–946.

27 Higginson IJ, Evans CJ, Grande G, *et al.* Evaluating complex interventions in end of life care: the MORECare statement on good practice generated by a synthesis of transparent expert consultations and systematic reviews. *BMC Med* 2013; 11: 111.

28 Bestall JC, Paul EA, Garrod R, *et al.* Usefulness of the Medical Research Council (MRC) dyspnoea scale as a measure of disability in patients with chronic obstructive pulmonary disease. *Thorax* 1999; 54: 581–586.

29 Malterud K, Siersma VD, Guassora AD. Sample size in qualitative interview studies: guided by information power. *Qual Health Res* 2016; 26: 1753–1760.

30 Michie S, van Stralen MM, West R. The behaviour change wheel: a new method for characterising and designing behaviour change interventions. *Implement Sci* 2011; 6: 42.

31 Smart A, Harrison E. The under-representation of minority ethnic groups in UK medical research. *Ethn Health* 2017; 22: 65–82.

32 Broadbent E, Petrie KJ, Main J, *et al*. The brief illness perception questionnaire. *J Psychosom Res* 2006; 60: 631–637.

33 Sekhon M, Cartwright M, Francis JJ. Acceptability of healthcare interventions: an overview of reviews and development of a theoretical framework. *BMC Health Serv Res* 2017; 17: 88.

34 Oriani A, Dunleavy L, Sharples P, *et al.* Are the MORECare guidelines on reporting of attrition in palliative care research populations appropriate? A systematic review and meta-analysis of randomised controlled trials. *BMC Palliat Care* 2020; 19: 6.

35 Farquhar MC, Prevost AT, McCrone P, *et al.* Is a specialist breathlessness service more effective and cost-effective for patients with advanced cancer and their carers than standard care? Findings of a mixed-method randomised controlled trial. *BMC Med* 2014; 12: 194.