Integrating Comprehensive Geriatric Assessment for people with COPD and frailty starting pulmonary rehabilitation: the Breathe Plus feasibility trial protocol

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Take home message:
This protocol describes the first study testing the feasibility of integrating a comprehensive geriatric assessment alongside pulmonary rehabilitation for people with both COPD and frailty, and the appropriate trial methods to test its effectiveness.

Abstract

Rationale: One in five people with COPD also live with frailty. People living with both COPD and frailty are at increased risk of poorer health and outcomes, and face challenges to completing pulmonary rehabilitation. Integrated approaches that are adapted to the additional context of frailty are required.

Aim: To determine the feasibility of conducting a randomised controlled trial of an integrated comprehensive geriatric assessment for people with COPD and frailty starting pulmonary rehabilitation.

Methods: Multicentre, mixed-methods, assessor-blinded, randomised, parallel group, controlled feasibility trial ('Breathe Plus'; ISRCTN13051922). We aim to recruit 60 people aged ≥50 with both COPD and frailty referred for pulmonary rehabilitation. Participants will be randomised 1:1 to receive usual pulmonary rehabilitation, or pulmonary rehabilitation with an additional comprehensive geriatric assessment. Outcomes (physical, psycho-social and service use) will be measured at baseline, 90 days and 180 days. We will also collect service and trial process data, and conduct qualitative interviews with a sub-group of participants and staff. We will undertake descriptive analysis of quantitative feasibility outcomes (recruitment, retention, missing data, blinding, contamination, fidelity), and framework analysis of qualitative feasibility outcomes (intervention acceptability and theory, outcome acceptability). Recommendations on progression to a full trial will comprise integration of quantitative and qualitative data, with input from relevant stakeholders. This study has been approved by a UK Research Ethics Committee (Ref:19/LO/1402).

Summary: This protocol describes the first study testing the feasibility of integrating a comprehensive geriatric assessment alongside pulmonary rehabilitation and testing this intervention within a mixed-methods randomised controlled trial.

Key words:

Respiratory disease, frailty, rehabilitation, integrated care, trial protocols, feasibility trials, mixed-methods

Introduction

One in five people with COPD are living with frailty (1). Frailty is broadly understood as a multidimensional syndrome characterised by decreases in reserve and diminished resistance to stressors (2). People with both COPD and frailty are at increased risk of mortality(3, 4) and have increased rates of hospitalisation (4) compared to non-frail counterparts. They experience poorer physical function, health status and quality of life (4, 5), and have increased anxiety and depression symptoms (6).

Pulmonary rehabilitation typically comprises twice-weekly, supervised, outpatient exercise sessions (involving progressive resistance and aerobic training based on individualised prescriptions) over 6-12 weeks, plus education to support self-management (7). Importantly, pulmonary rehabilitation is equally, if not more, efficacious in people living with COPD and frailty: it can improve breathlessness, exercise performance, self-reported physical activity levels, anxiety and depression symptoms, and health status (6, 8), as well as reducing frailty (6, 9). However, people living with both COPD and frailty are less likely to start and complete pulmonary rehabilitation (6). Development and testing adapted approaches encouraging engagement with pulmonary rehabilitation and improving outcomes for this population are therefore high priorities.

To develop an adapted approach and our preliminary underpinning intervention theory, we conducted qualitative interviews with people living with both COPD and frailty referred for pulmonary rehabilitation (10). Participants described continually striving to adapt to multidimensional losses associated with COPD and frailty, and variability in support received. While all were initially motivated to engage in pulmonary rehabilitation, changeable health and disruptions (e.g. exacerbations, worsening comorbidities, other appointments) could interfere with, and sometimes erode, their motivation and ability to attend. We then conducted a realist review to understand how exercise-based interventions for people with COPD might better address the context of frailty (11). We found that successful exercise-based interventions for this group might need to foster trusting relationships with participants and a shared understanding of their priorities, individualise content to match priorities, have capacity to address multidimensional losses, and offer a flexible service delivery approach. Strategies to enable these mechanisms were identified, including a potential role for Comprehensive Geriatric Assessment (CGA).

CGA is a process incorporating a comprehensive, multidimensional review of a person's medical, psychological, functional and social capability, in order to develop individual recommendations and a care plan (12). This typically involves treating any reversible causes, reviewing medicines including the impact of polypharmacy, providing nutritional support, cognitive assessment, and offering exercise training (12). CGAs reduce functional dependency and mortality for older adults across inpatient (13) and outpatient settings (14). In frail older adults, coordinated care based on CGA recommendations can improve quality of life and function, and reduce hospital admissions (15). When introduced alongside other treatments, CGAs may increase capacity to benefit: pre-surgery CGAs can reduce post-operative complications and recovery (16) and CGAs delivered prior to chemotherapy are associated with increased tolerance and completion (17). Recent work in inpatient respiratory rehabilitation has also suggested improved disease-specific health-status and reduced exacerbations(18) following a CGA-directed approach.

Besides exercise, most core components of a CGA are not routinely addressed by outpatient pulmonary rehabilitation (7). Integrating these two evidence-based interventions may therefore be of value to people living with both COPD and frailty. In our preliminary intervention theory (Figure

1), we propose that addition of a CGA at the start of pulmonary rehabilitation may help foster some of the mechanisms deemed important by our development work (10, 11). By fostering therapeutic alliance and tailored, multidimensional care recommendations, this approach may increase engagement with self-management and supportive services, including pulmonary rehabilitation, and contribute to improved health and function through increased reserves and adaptation.

[INSERT FIGURE 1]

The proposed intervention is inherently complex: it includes multiple interacting components and relies on complex behaviours from participants and professionals (19). Moreover, we will be working within complex systems, made up of individual, organisational and societal influences (20). As such there are multiple uncertainties around the feasibility and acceptability of the intervention, and how best to evaluate its impact, that must be addressed prior to an effectiveness trial (20). This study aims to determine the feasibility of conducting a randomised controlled trial of an integrated CGA for people with COPD and frailty starting pulmonary rehabilitation. Objectives are shown in Table 1.

Table 1: Study objectives

#	Objective
1	To explore the acceptability of the intervention for participants and staff
2	To define, and understand the fidelity of, integrating a comprehensive geriatric assessment, including how it differs from and impacts on usual care
3	To refine the intervention theory around integration of a comprehensive geriatric assessment for this population
4	To estimate the appropriateness of the proposed eligibility criteria and study processes in successfully recruiting and retaining participants in the trial
5	To estimate risk of contamination between trial groups and unblinding in the trial
6	To explore the appropriateness and acceptability of proposed outcome measures and trial processes for participants and staff

Methods

Design

The Breathe Plus feasibility trial will use a multicentre, mixed-method randomised controlled, assessor-blind trial design. Participants will be randomised 1:1 to two parallel groups: usual care, or usual care plus a CGA. Quantitative intervention and trial data (including process data and participant outcome measures at baseline, 90 days and 180 days) will be collected alongside qualitative interview data from a subset of participants and staff (Figure 2).

[INSERT FIGURE 2]

Setting

Participants will be recruited from three outpatient pulmonary rehabilitation services based in hospitals in London, UK. Data collection will take place at participants' place of preference, typically: the hospitals, the university, participants' place of residence, or via telephone.

Participants

Participants will include people living with both COPD and frailty referred for outpatient pulmonary rehabilitation. Full inclusion/exclusion criteria are shown in Table 2.

Table 2: Inclusion and Exclusion Criteria

Inclusion criteria	**Exclusion criteria**
Adults aged 50 years or older	Lacking mental capacity to provide informed consent
Physician diagnosis of chronic obstructive pulmonary disease (in line with GOLD criteria(21))	Unable to communicate verbally and respond to questions in written English and no interpreters to enable this
Referred for outpatient pulmonary rehabilitation (in line with BTS guidance(7))*	Receiving specialist geriatric services involving a geriatric doctor in previous or upcoming month
Rockwood Clinical Frailty Scale score of ≥5 (22)	

GOLD = Global initiative for chronic Obstructive Lung Disease; BTS = British Thoracic Society
**During the coronavirus pandemic, this will be inclusive of standard pulmonary rehabilitation available, including supported home-based exercise programmes*

The Clinical Frailty Scale is easy to administer in clinical settings and has been shown to be reliable and comparable to the Frailty Phenotype (23). As the Clinical Frailty Scale should only be used after a formal clinical assessment (24) it will be incorporated alongside usual pre-pulmonary rehabilitation assessments. The research team will provide professionals using the Clinical Frailty Scale with training, drawing on published resources (25).

Sampling and recruitment

We will sample participants consecutively from people attending pre-pulmonary rehabilitation assessments. These assessments may take place remotely during the coronavirus pandemic. Pulmonary rehabilitation staff at each site will check peoples' eligibility during this assessment and introduce them to the study if applicable. Those interested in participating will receive a participant information sheet, and a researcher will discuss the study with them in detail. Those agreeing to participate will be asked to provide a record of consent. We anticipate recruitment of our target sample in 12 months across three sites.

Interventions

Usual care:

All participants will continue their planned pulmonary rehabilitation course (typically at least twice-weekly supervised outpatient exercise sessions plus education for at least six weeks; may include amended remote-facilitated rehabilitation during the coronavirus pandemic). Usual care may also include interactions with specialist and non-specialist health and social care as required (e.g. respiratory consultant, GP, other specialists that support comorbid conditions, emergency and/or hospital care, and care from integrated COPD nursing teams that support hospital discharge and management of exacerbations at home). All usual care contacts are permitted in both trial arms and will be recorded as feasibility trial data.

Comprehensive geriatric assessment:

In addition to usual care, the intervention group will receive a CGA as soon as possible following completion of baseline measures, ideally prior to starting pulmonary rehabilitation. CGA is a process comprising a comprehensive assessment, development of a tailored care plan, and follow-up as required. We will encourage teams to work with their local materials (e.g. clinic proformas) to align intervention delivery with their usual practice.

The CGA will be led by a geriatric consultant. The initial appointment will typically be delivered as a one-to-one face-to-face appointment in an outpatient clinic, lasting approximately one hour (during the coronavirus pandemic, remote delivery via video/phone may also be used). This will include a full medical assessment and history, and typically a review of functional and psychosocial issues, management of geriatric syndromes (e.g. frailty, falls, sarcopenia, incontinence, malnutrition, sensory impairment) and/or advance care planning, as relevant for the person. A resulting individualised care plan will be communicated back to the participant and relevant health care professionals (e.g. GP, pulmonary rehabilitation team), for actioning. In all cases, tailoring of the comprehensive geriatric assessment, subsequent follow-up, and decision to discharge will be led by the geriatrician.

Support will be provided for travel where necessary. For two recruiting sites, the geriatric clinic is at the same hospital as the pre-pulmonary rehabilitation assessment. For one recruiting site, the geriatric clinic is at a different, nearby hospital.

Feasibility outcomes and progression criteria

Our primary feasibility outcomes relate to intervention fidelity and acceptability. Table 3 lists all feasibility outcomes, contributing data and progression criteria to full trial.

Table 3: Breathe Plus feasibility outcomes, contributing data and progression criteria

Obj.	Feasibility outcomes	Contributing data	Progression criteria		
			Green	**Amber**	**Red**
1	*Acceptability of the intervention to participants and staff	Participant & staff interviews	Reported as acceptable (or can be with minimal modification)	Reported as acceptable with modification	Intervention not acceptable
2	*Fidelity of delivery of recommendations from the CGA	Participant questionnaires & CGA service data	≥80% of recommendations implemented	79-50%	<50%
	Defining what and how many recommendations are made in the CGA	CGA Service data	*NA, descriptive*		
	Defining what does usual care comprise	Participant questionnaires & PR service data	*NA, descriptive*		
3	Theoretical underpinning of the intervention	Participant & staff interviews	*NA, descriptive*		
4	Identification and recruitment of eligible participants	Screening & recruitment log	≥20% screened eligible ≥60% eligible recruited	19-10% 59-40%	<10% <40%
	Participant retention at follow-up	Participation data	≥75% retained at 3 months ≥60% retained at 6 months	74-60% 59-40%	<60% <40%
5	Contamination of the control group	CGA service data	≤10% participants receive a CGA within usual care	11-20%	>20%
	Success of data collector blinding	Participation data	Blinding maintained for ≥85% participants	84-70%	<70%
6	Acceptability of outcome measures and their timing	Participant questionnaires & interviews	Missing data of ≤10% for each measure. Participant-reported acceptability.	11-25% Some	>25% None

CGA = Comprehensive Geriatric Assessment, PR = Pulmonary Rehabilitation, NA = Not Applicable

* primary focus; Traffic-light progression criteria(26) - Green: likely no concerning issues, Amber: potentially remediable issues , Red: potentially intractable issues

Data collection

Service and trial process data

Process data will be used to understand intervention delivery, potential impacts on usual care, and trial design appropriateness.

- *CGA service delivery (*intervention group participants only)*:* CGA date, recommendations, and follow-up, including (where applicable) when and who completed the recommendations.

- *Pulmonary rehabilitation service delivery* (all participants): number of pulmonary rehabilitation sessions attended, adaptations made (e.g. dose reduction, delays in completion), and completion of post-pulmonary rehabilitation assessment.

- *Trial process data:* trial screening and recruitment rates, participation at each timepoint, mode of data collection, missing data, and unblinding.

Participant characteristics and clinical outcomes

Baseline demographic characteristics will be obtained through routinely collected data from the pulmonary rehabilitation teams, and self-reported questionnaires. These will include personal characteristics (age, sex, ethnicity), health and function (Forced expiratory volume in one second [FEV1] % predicted, Medical Research Council [MRC] dyspnoea, exacerbations, six-minute walk test and/or incremental shuttle walk test, comorbidities, smoking status) and social factors (gender, living alone or with others, presence of an informal carer, being an informal carer, housing status, formal education level, English Indices of Social Deprivation).

The clinical outcome measures reflecting multiple domains (Table 4) will be collected at baseline, 90 days and 180 days post-randomisation. In most cases, questionnaires will be completed with support from the researcher, but self-completion with return by post will also be allowed. While an in-person visit will be sought, all outcomes except physical frailty could be collected by phone if required. When completed by phone, participants will be sent a copy of the questionnaire to view during the call.

Table 4: Clinical outcome measures

Domain	Measure	Description
Physical frailty	Short Physical Performance Battery (SPPB) (27)	Incorporates 4m gait speed, 5 sit-to-stands, and static balance tests. It takes approximately 10-15 minutes to complete, requires a floor mark for the gait-speed test, chair for sit-to-stand, and a timer, and results in a score from 0-12 (≤ 7indicating frailty, 8-9 pre-frailty, and 10-12 robustness).
Health-related quality of life	Chronic Respiratory Questionnaire (CRQ-SR) (28)	This scale contains 20 items measuring the impact of chronic respiratory disease across four domains: dyspnoea, mastery, fatigue, and emotional function. Each item is scored from 1-7, and the mean score across each domain is calculated. Higher scores indicate better health status.
Activities of daily living	Manchester Respiratory Activities of Daily Living questionnaire (29).	This measure includes 21 self-report items across four domains: mobility, kitchen activities, domestic tasks, and leisure activities. Most items are scored 0-1 based on responses of doing tasks 'not at all', 'with help', 'alone with difficulty' or 'alone easily' and total scores range from 0 to 21, where 21 indicates no impairment in daily activities.
Health status	Euro-Qol 5D-5L	This measure contains 5 descriptive items (mobility, self-care, usual activities, pain, and anxiety/depression) with a five-point scale from 'no problems' to 'unable/extreme problems', and a visual analogue scale asking participants to rate their health from 0 (worst health imaginable) to 100 (best health imaginable). Descriptive item scores are converted into a single index value for health status, where a high value represents higher health status. Scores would also contribute to health economic analyses in a future effectiveness study.
Anxiety and depression	Hospital Anxiety and Depression Questionnaire (HADS)(30)	This is a 14-item questionnaire with two subscales: anxiety (7 items) and depression (7 items). Items are scored on a scale of 0 to 3. Items are summed creating a maximum score of 21 on each subscale, where higher scores indicate higher levels of symptoms of anxiety or depression.
Loneliness	De Jong Gierveld Loneliness Scale (6-item) (31)	This shortened version includes 3 items measuring social loneliness, and 3 items measuring emotional loneliness, scored as 0 or 1. When summed, a higher score indicates higher levels of loneliness.
Service use	Client Service Receipt Inventory (CSRI) (32)	This measure asks participants about their contacts with hospital and community health care services, any investigations or diagnostic tests, help from informal carers, and medication and equipment used, over the past 3 months. This measure would also contribute to health economic analysis in a future effectiveness study.

Nested qualitative interviews

Nested semi-structured qualitative interviews will be conducted with a sub-sample of participants and staff to address feasibility objectives 1 (intervention acceptability), 3 (theoretical underpinning) and 6 (outcome acceptability)(Table 3).

- Participant interviews: We will interview approximately 10 intervention group participants following their second (90-day) data collection timepoint. Interviewing intervention participants only was deemed most appropriate as our primary feasibility objectives relate to intervention acceptability. Purposive sampling will be used to obtain maximum variation in relation to site and intervention fidelity, with consideration of diversity in terms of living status, outcomes, and questionnaire completion where possible. Informal carers will be welcome to participate alongside participants. Interviews will explore experiences of the intervention and trial participation.

- Staff interviews: We will interview approximately 5 staff involved in the delivery of the trial. Purposive sampling will be used to obtain maximum variation in relation to site and team type (e.g. pulmonary rehabilitation, geriatrics). Interviews will explore experiences of the trial and perceptions of the intervention.

Interview schedules will be informed by the theoretical framework of acceptability (33) and reviewed by relevant stakeholders (people with relevant clinical, academic and/or personal experience). Interviews will be digitally audio-recorded. Field notes will record interview flow, contextual factors, participant responses, and personal reflections. Stopping of recruitment will be based on sufficiency of information power (34) to answer the feasibility objectives.

Sample size

We intend to recruit a total of 60 participants (30 to the intervention group, 30 to the control group). This sample size was deemed to give an acceptable level of precision for our quantitative feasibility outcomes (35).

Randomisation & allocation concealment

Randomisation will occur as soon as possible following consent form completion and baseline assessment. Eligible participants will be randomly allocated 1:1 to the intervention or control group.

Randomisation method of minimisation was chosen with factors defined by site (1, 2 and 3), breathlessness (MRC dyspnoea 2-3 and 4-5), exacerbations (≥2 and <2 in the past year) and living alone status (yes and no), along with an algorithm that contains an element of simple randomisation in order to preserve pre-randomisation allocation concealment.

The authorised researchers will randomise participants via the independent web based randomisation system, run by the King's Clinical Trials Unit, which will automatically email the randomisation result to relevant members of the research team (e.g. chief investigator, research assistant) in a pre-specified blinded or unblinded format, depending on their role. An unblinded member of the research team will inform participants of their group allocation by phone.

Blinding

It will not be possible to blind participants and intervention providers. Blinded researchers will collect follow-up clinical outcome assessments and complete the quantitative analysis.

Analysis

Quantitative data

Data will be entered by authorised researchers into a secure password-protected web-based Elsevier MACRO Electronic Data Capture system created in collaboration with the King's Clinical Trials Unit, which will capture a full audit trail of data entry and amendments. At trial end, following verification of data accuracy, the dataset will be locked for analysis.

A single intention-to-treat analysis will occur. Feasibility outcomes (Table 3) will be described using proportions and corresponding 95% confidence intervals, or, for continuous variables as means/medians and SD/range, depending on the data distribution. Where source data is not already quantified (e.g. CGA service notes), inductive content analysis will be used to summarise this information.

Baseline characteristics of the intervention and control participants will be summarised using descriptive statistics. Participant flow through the trial will be reported in a Consolidated Standards of Reporting Trials (CONSORT) flow diagram. In keeping with the feasibility aims, clinical outcomes will be described, but no inferential statistics used. Safety data will also be summarised.

Qualitative data

Qualitative interview data will be transcribed verbatim and link-anonymised. Framework analysis(36) will be used to explore the three qualitative feasibility outcomes (intervention acceptability, intervention theory, and outcome acceptability; Table 3).

The analysis process will begin with familiarisation with transcripts and field notes. An analytical framework will then be developed drawing deductively on the research objectives and relevant theoretical frameworks (including our preliminary intervention theory). The analytical framework will also be open to inductively-generated participant-raised issues. This framework will be revised based on revisiting the original data to ensure fair interpretation, engagement with wider relevant literature that may deepen our understanding, and review by relevant stakeholders to encourage a more nuanced reading. The analytical framework will then be systematically applied to the dataset, charting summarised data in a case-by-theme matrix. We will then map and interpret key findings and analytical themes in relation to the feasibility outcomes. The qualitative findings will be presented using a narrative approach, incorporating illustrative participant quotes. Although presented as a linear process, we will move forwards and backwards through these stages as thinking develops and changes (36). Qualitative data will be mixed with the quantitative data during interpretation and reporting.

Integration & recommendations for progression to a full trial

Progression to the full trial will be determined based on feasibility trial results meeting pre-defined criteria (Table 3) within the context of qualitative data (26); in particular, where the qualitative data provides additional understanding and potential remedies for data falling in the amber/red zones.

The data will be considered alongside views of key stakeholders including trial team members, clinicians involved in its delivery, and people affected by COPD and frailty. Conclusions and key recommendations in relation to each feasibility outcome will be reported with justifications, to aid transparency around the final decision.

Monitoring adverse events

All adverse events will be recorded in study database and monitored for duration of the trial. The study may be terminated if safety or ethical concerns are raised over the intervention and/or trial processes, or if there is a noticeable increase in number of deaths, emergency attendances or hospital admissions in either arm, as reviewed and recommended by joint trial management group / data monitoring committee at bi-annual meetings or ad-hoc meetings (if necessary).

Patient and public involvement

Public involvement members affected by COPD and frailty, including members of our project team, and members of other relevant local public involvement groups (e.g. at the Cicely Saunders Institute, Harefield Breathing Group, and the local Biomedical Research Centre Respiratory group), have been involved in the intervention development work (10, 11) and continue to contribute to this feasibility trial. To date, we have received public involvement feedback on the trial name, recruitment processes, participant information materials, outcome measures, and qualitative interview topic guides. Ongoing involvement includes discussing trial progress, troubleshooting arising challenges, assisting with the qualitative analysis, seeking their reflections and interpretations in relation to findings, and advising on dissemination. At the end of the trial we will use the Guidance for Reporting Involvement of Patients and the Public short form(37) to guide a critical reflection on the public involvement in the study.

Ethics

This study has been approved by the London City and East Research Ethics Committee (Ref. 19/LO/1402). All participants provide a record of informed consent for their participation.

Protocol version and amendments

This paper reflects version 3.0 of the study protocol dated 25/06/2020. We have made two protocol amendments to date. Based on our experience with the first few participants, we allowed qualitative interviews to occur earlier (from 90 days onwards, rather than 180 days) to facilitate participation and recall. Due to restrictions on in-person contacts during the coronavirus pandemic, we have also expanded data collection, usual care and intervention procedures to be inclusive of remote methods.

Dissemination

A plain-English summary will be sent to participants opting to receive this on their consent form. We will submit the results for publication in an open-access peer-reviewed journal, with authorship eligibility according to the International Committee of Medical Journal Editors criteria(38). Findings will be reported following the CONSORT guidelines for pilot and feasibility trials(39) and Template for Intervention Description and Replication statement(40). We will further share findings with clinical, academic, and public stakeholders across websites, social media, and presentations at local, national and international meetings. The full study protocol and anonymised data will be available on request.

Discussion

There is growing recognition of the potential for integration between geriatric and respiratory care (41, 42). The Breathe Plus feasibility trial will test the feasibility of integrating two evidence-based approaches: comprehensive geriatric assessment and pulmonary rehabilitation. We hope that this will both add value to rehabilitation services, and better address frailty and its consequences in people with respiratory disease.

While bringing together two areas of effective respiratory and geriatric care seems a clear opportunity to improve outcomes for people with COPD and frailty, in practice it requires integration of multiple complex systems. This preliminary work is therefore essential to address the uncertainties surrounding joining of established practices, potential benefits and burdens for participants and staff, and whether our proposed methods would be capable of capturing such impacts in a future effectiveness trial. It has already been necessary to add some flexibility in our methods due to coronavirus-related disruptions, and it may be that further adaptations to this changing context are required. However, by exploring the intervention theory alongside processes and outcomes, we hope we can explore the impact of such changes and inform further context-specific implementation should this approach be successful.

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References

1. Marengoni A, Vetrano DL, Manes-Gravina E, Bernabei R, Onder G, Palmer K. The Relationship Between COPD and Frailty: A Systematic Review and Meta-Analysis of Observational Studies. Chest. 2018;154(1):21-40.
2. Rodriguez-Manas L, Feart C, Mann G, Vina J, Chatterji S, Chodzko-Zajko W, et al. Searching for an operational definition of frailty: a Delphi method based consensus statement: the frailty operative definition-consensus conference project. J Gerontol A Biol Sci Med Sci. 2013;68(1):62-7.
3. Galizia G, Cacciatore F, Testa G, Della-Morte D, Mazzella F, Langellotto A, et al. Role of clinical frailty on long-term mortality of elderly subjects with and without chronic obstructive pulmonary disease. Aging Clin Exp Res. 2011;23(2):118-25.
4. Kennedy CC, Novotny PJ, LeBrasseur NK, Wise RA, Sciurba FC, Benzo RP. Frailty and Clinical Outcomes in Chronic Obstructive Pulmonary Disease. Annals of the American Thoracic Society. 2019;16(2):217-24.
5. Kusunose M, Oga T, Nakamura S, Hasegawa Y, Nishimura K. Frailty and patient-reported outcomes in subjects with chronic obstructive pulmonary disease: are they independent entities? BMJ Open Respir Res. 2017;4(1):e000196.
6. Maddocks M, Kon SS, Canavan JL, Jones SE, Nolan CM, Labey A, et al. Physical frailty and pulmonary rehabilitation in COPD: a prospective cohort study. Thorax. 2016;71(11):988-95.
7. British Thoracic Society. Quality Standards for Pulmonary Rehabilitation in Adults. British Thoracic Society Reports. 2014;6(2):1-32.
8. Blindenbach S, Vrancken JWFA, van der Zeijden H, Reesink HJ, Brijker F, Smalbrugge M, et al. [Effects of Geriatric COPD rehabilitation on hospital admissions and exercise tolerance: a retrospective observational study]. Effecten van geriatrische COPD-revalidatie op ziekenhuisopnames en inspanningstolerantie: een retrospectief observationele studie. 2017;48(3):112-20.
9. Mittal N, Raj R, Islam E, Nugent K. Pulmonary rehabilitation improves frailty and gait speed in some ambulatory patients with chronic lung diseases. The Southwest Respiratory and Critical Care Chronicals. 2015;3(12):2-10.
10. Brighton LJ, Bristowe K, Bayly J, Ogden M, Farquhar M, Evans CJ, et al. Experiences of pulmonary rehabilitation in people living with COPD and frailty: a qualitative interview study. Annals of the American Thoracic Society. 2020:e-pub before print, doi:10.1513/AnnalsATS.201910-800OC
11. Brighton LJ, Evans CJ, Man W, Maddocks M. Improving exercise-based interventions for people living with both COPD and frailty: a realist review. International journal of chronic obstructive pulmonary disease. 2020(15):841-55.
12. Turner G, Clegg A. Best practice guidelines for the management of frailty: a British Geriatrics Society, Age UK and Royal College of General Practitioners report. Age Ageing. 2014;43(6):744-7.
13. Ellis G, Whitehead MA, Robinson D, O'Neill D, Langhorne P. Comprehensive geriatric assessment for older adults admitted to hospital: meta-analysis of randomised controlled trials. BMJ. 2011;343:d6553.
14. Reuben DB, Frank JC, Hirsch SH, McGuigan KA, Maly RC. A randomized clinical trial of outpatient comprehensive geriatric assessment coupled with an intervention to increase adherence to recommendations. J Am Geriatr Soc. 1999;47(3):269-76.
15. Boult C, Green AF, Boult LB, Pacala JT, Snyder C, Leff B. Successful models of comprehensive care for older adults with chronic conditions: evidence for the Institute of Medicine's "retooling for an aging America" report. J Am Geriatr Soc. 2009;57(12):2328-37.
16. Vidan M, Serra JA, Moreno C, Riquelme G, Ortiz J. Efficacy of a comprehensive geriatric intervention in older patients hospitalized for hip fracture: a randomized, controlled trial. J Am Geriatr Soc. 2005;53(9):1476-82.
17. Kalsi T, Babic-Illman G, Ross PJ, Maisey NR, Hughes S, Fields P, et al. The impact of comprehensive geriatric assessment interventions on tolerance to chemotherapy in older people. Br J Cancer. 2015;112(9):1435-44.

18. van Dam van Isselt EF, van Eijk M, van Geloven N, Groenewegen-Sipkema KH, van den Berg J-WK, Nieuwenhuys CMA, et al. A Prospective Cohort Study on the Effects of Geriatric Rehabilitation Following Acute Exacerbations of COPD. Journal of the American Medical Directors Association. 2019;20(7):850-6.e2.
19. Craig P, Dieppe P, Macintyre S, Michie S, Nazareth I, Petticrew M. Developing and evaluating complex interventions: the new Medical Research Council guidance. Brit Med J. 2008;337.
20. Fletcher A, Jamal F, Moore G, Evans RE, Murphy S, Bonell C. Realist complex intervention science: Applying realist principles across all phases of the Medical Research Council framework for developing and evaluating complex interventions. Evaluation (Lond). 2016;22(3):286-303.
21. Global Initiative for Chronic Obstructive Lung Disease. Pocket guide to COPD diagnosis, management, and prevention: a guide for health care professionals. Retrieved from: https://goldcopd.org/wp-content/uploads/2020/03/GOLD-2020-POCKET-GUIDE-ver1.0_FINAL-WMV.pdf, accessed 9 July 2020; 2020.
22. Rockwood K, Song X, MacKnight C, Bergman H, Hogan DB, McDowell I, et al. A global clinical measure of fitness and frailty in elderly people. CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne. 2005;173(5):489-95.
23. Islam A, Muir-Hunter SW, Speechley M, Montero-Odasso M. Facilitating Frailty Identification: Comparison of Two Methods among Community-Dwelling Order Adults. The Journal of frailty & aging. 2014;3(4):216-21.
24. British Geriatrics Society. Recognising frailty. Retrieved from https://www.bgs.org.uk/resources/recognising-frailty, accessed June 2019. ; 2014.
25. The Ottawa Hospital. Clinical Frailty Scale (CFS) Training Module https://rise.articulate.com/share/deb4rT02lvONbq4AfcMNRUudcd6QMts3#/, accessed 22 October 20192019 [
26. Avery KNL, Williamson PR, Gamble C, Connell Francischetto E, Metcalfe C, Davidson P, et al. Informing efficient randomised controlled trials: exploration of challenges in developing progression criteria for internal pilot studies. Bmj Open. 2017;7(2):e013537.
27. Guralnik JM, Simonsick EM, Ferrucci L, Glynn RJ, Berkman LF, Blazer DG, et al. A Short Physical Performance Battery Assessing Lower Extremity Function: Association With Self-Reported Disability and Prediction of Mortality and Nursing Home Admission. Journal of Gerontology. 1994;49(2):M85-M94.
28. Williams JEA, Singh SJ, Sewell L, Guyatt GH, Morgan MDL. Development of a self-reported Chronic Respiratory Questionnaire (CRQ-SR). Thorax. 2001;56(12):954-9.
29. Yohannes AM, Roomi J, Winn S, Connolly MJ. The Manchester Respiratory Activities of Daily Living questionnaire: development, reliability, validity, and responsiveness to pulmonary rehabilitation. J Am Geriatr Soc. 2000;48(11):1496-500.
30. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. Acta psychiatrica scandinavica. 1983;67(6):361-70.
31. Gierveld JDJ, Tilburg TV. A 6-item scale for overall, emotional, and social loneliness: Confirmatory tests on survey data. Research on aging. 2006;28(5):582-98.
32. Beecham J, Knapp M. Costing psychiatric interventions. In: Thornicroft G, editor. Measuring mental health needs. 2 ed2001. p. 200-24.
33. Sekhon M, Cartwright M, Francis JJ. Acceptability of healthcare interventions: an overview of reviews and development of a theoretical framework. BMC health services research. 2017;17(1):88.
34. Malterud K, Siersma VD, Guassora AD. Sample Size in Qualitative Interview Studies: Guided by Information Power. Qual Health Res. 2015.
35. Hooper R. Justifying sample size for a feasibility study. Research Design Service. National Institute for Health Research London. Available from https://www.rds-london.nihr.ac.uk/wpcms/wp-content/uploads/2019/02/Justifying-sample-size-for-feasibility-study-updated-22-Feb-2019.pdf, accessed 18 September 2020.
36. Ritchie J, Spencer L. Qualitative data analysis for applied policy research. In: Bryman A, Burgess B, editors. Analyzing Qualitative Data. 1 ed: Routledge; 1994. p. 173-94.
37. Staniszewska S, Brett J, Simera I, Seers K, Mockford C, Goodlad S, et al. GRIPP2 reporting checklists: tools to improve reporting of patient and public involvement in research. BMJ. 2017;358:j3453.

38. International Committee of Medical Journal Editors. Defining the Role of Authors and Contributors. Retreived from: http://www.icmje.org/recommendations/browse/roles-and-responsibilities/defining-the-role-of-authors-and-contributors.html, accessed 23 July 2020; 2020.
39. Eldridge SM, Chan CL, Campbell MJ, Bond CM, Hopewell S, Thabane L, et al. CONSORT 2010 statement: extension to randomised pilot and feasibility trials. Pilot Feasibility Stud. 2016;2:64.
40. Hoffmann TC, Glasziou PP, Boutron I, Milne R, Perera R, Moher D, et al. Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide. BMJ. 2014;348:g1687.
41. Brighton LJ, Bone AE, Maddocks M. Supportive and palliative care for people with chronic respiratory disease and frailty. Current Opinion in Supportive and Palliative Care 2020;14(3):206-12.
42. Iyer AS, Curtis JR, Meier DE. Proactive Integration of Geriatrics and Palliative Care Principles Into Practice for Chronic Obstructive Pulmonary Disease. JAMA Intern Med. 2020.

Figures

Figure 1: Preliminary intervention theory of integrating a comprehensive geriatric assessment for people with COPD and frailty starting pulmonary rehabilitation

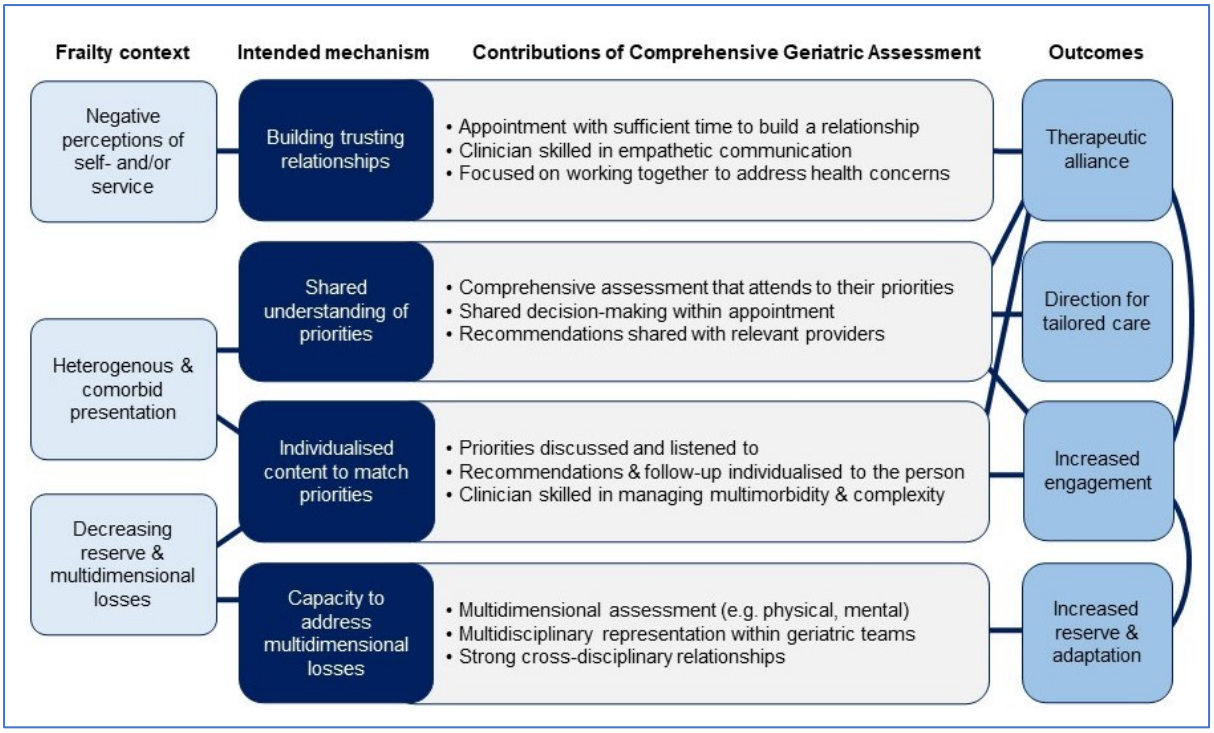

Figure 2: Overview of the Breathe Plus feasibility trial design