Breathing REtraining for people with AsTHma and breathing pattern disorder (BREATH)

1 Background and rationale

Asthma is one of the most common long-term conditions, with a UK lifetime prevalence of 9.8 million people [1]. Current NICE guidelines for asthma focus on pharmacological management[2]. However, at least 1/3 of patients with asthma also present with breathing pattern disorder (BPD) [3, 4], a term used to characterise breathlessness resulting from suboptimal control of respiratory muscles [4]. Pharmacological management does not address the muscular control of breathing, and this might explain why a high proportion of people with asthma continue to experience breathlessness, despite taking medication [5]. Furthermore, patients with asthma, who also have BPD, are known to have poorer asthma control [6], increased anxiety [7] and lower quality of life [6]. It is therefore critical to develop interventions which can bring about a long-term improvement in the muscular control of breathing that could be integrated into NHS pathways.

The term breathing pattern disorder covers a spectrum of suboptimal breathing patterns. These range from hyperventilation, periodic deep sighing, thoracic dominant breathing, forced abdominal expiration and thoracic-abdominal asynchrony [4, 8]. These changes in breathing mechanics result from a change in respiratory muscular control. However, control of respiratory musculature will be affected by changes in stiffness and low-level muscle contraction (muscle tone) in postural muscles. For example, increased stiffness (or tone) in the abdominal muscles will reduce the capacity for the rib cage to move superiorly relative to the pelvis [9] and will limit outward expansion of the abdominal cavity. This, in turn, will affect rib movement and reduce the capacity for the diaphragm to move downwards, changes which are likely to lead to altered breathing patterns, such as thoracic dominant breathing and thoracic-abdominal asynchrony. Given this link between postural muscle control and respiratory function, it is important that treatments for asthma with BPD include training to improve postural muscle activity.

Alongside breathing difficulties, people with asthma report high rates of musculoskeletal comorbidity[10]. For example, studies have highlighted that approximately 30% of people with asthma experience chronic neck/back pain [11]. Postural abnormalities, such as increase neck protraction and thoracic curvature [10, 12] are also associated with asthma. Taken together, these findings point to an alteration in postural muscle control in asthma, a phenomenon which is likely to predispose people to BPD. Another common comorbidity in asthma is gastro-oesophageal reflux disease (GORD). While only 4% of people with GORD present with asthma, 51% of people with asthma present with hiatal hernia and 37% with oesophagitis [13]. There is well-established link between elevated intra-abdominal pressure, disruption of the esophagogastric junction and gastroesophageal reflux [14]. Furthermore, research has shown that such elevated intra-abdominal pressure results from coactivation of the diaphragm and abdominal muscles [15]. Again, this finding supports the idea of altered postural muscle control in people with asthma+BPD and therefore the need to develop treatments which can optimise postural muscle activity.

Research has consistently demonstrated a strong link between psychological factors and asthma control and symptoms [16]. For example, both fear of physical sensations [17] as well as dysfunctional cognitions (thoughts and beliefs) about asthma are associated with poorer asthma control [18]. In people with asthma, BPD has been shown to be associated with anxiety and depression [16]. Indications are that poorer cognitions about BPD are also associated with increased levels of anxiety and depression and greater impacts on daily living, demonstrating a strong link between psychological cognitions and health and wellbeing outcomes[19]. This relationship suggests a link between psychological factors and the muscle control of breathing and is consistent with the observation that people with chronic asthma have been observed to hyperventilate when instructed to recall a previous asthma attack [20]. These observations

highlight the need to incorporate psychological techniques into interventions for asthma+BPD to optimise the change in breathing behaviours and to sustain these changes.

Breathing is a behaviour [21] and as such, we propose the application of behavioural science to facilitate change and bring about new breathing behaviours. The use of behavioural theory and the incorporation of behavioural change techniques shows great promise in facilitating and maintaining change in a range of behaviours and health conditions [22]. We propose to use the Capability, Opportunity and Motivation - Behaviour (COM-B) model [23] which provides a robust and yet accessible approach to integrate into a multidisciplinary and multi-component approach and has been incorporated successfully in previous interventions [24].

We have developed a new physiotherapy treatment called "Cognitive Muscular Therapy" (CMT) [25]. CMT focuses on improving whole-body postural control rather than strengthening muscles. It aims to reduce overactivity in muscles around the abdomen, neck, shoulders, and back to achieve better posture balance. This postural retraining is combined with breathing re-education and integrated within a framework of psychologically informed physiotherapy. To enhance CMT, we integrate a breathing visualisation technique in which two 3D cameras are used to track the movement of the chest/abdomen/thorax and visualise the mechanics of breathing. Throughout the development of CMT, we have integrated a range of behaviour change techniques, which enable patients to sustain changes in pain and breathing behaviours. To date, we have created implementations of CMT for chronic musculoskeletal pain, including knee pain, low back pain and neck pain. We have also created an implementation of CMT for long-COVID which explicitly focuses on improving breathing control. Given our previous track record, we are confident that we can create and implementation of CMT for people with asthma+BPD.

The proposed study will be delivered through two stages:

1. Stage 1: Through a participatory design approach, we will iteratively develop an implementation of CMT which is appropriate for people with asthma+BPD.
2. Stage 2: Pilot the CMT intervention on 20 patients with asthma+BPD.

2 Study design

In stage 1, we will engage with both patients and physiotherapists, to develop, and refine the CMT intervention. Following initial focus groups, we will create a preliminary implementation of CMT which will be delivered to five patients. We will then seek feedback from these five patients and further refine the intervention. We will then deliver the intervention to another five patients and seek further feedback. With the final round of feedback, we will finalise the intervention so that it is ready for deliver in stage 2.

In stage 2, we will run an uncontrolled pilot study to explore the potential effectiveness of our finalised intervention for people with asthma+BPD. For this study, we will recruit 20 patients with asthma+BPD who each will receive CMT from our research physiotherapist. Clinical outcomes will be collected at baseline, after the final intervention session and then again at three months. In addition, mechanistic outcomes will be collected at baseline and after the final intervention session. To understand patient perceptions of the CMT treatment, we will perform a qualitative evaluation. We anticipate that the findings of this pilot study will inform the design of a follow-on feasibility trial which inform planning of a subsequent large-scale trial.

3 Recruitment and inclusion

In total, we plan to recruit 30 participants (n=10 for Stage 1 and n=20 for Stage 2) with asthma+BPD who satisfy the following inclusion/exclusion criteria.

Inclusion criteria:

1. Above 18 years old
2. GP diagnosis of asthma
3. Taking regular preventative asthma medications, e.g. steroid, LABA
4. Attended an asthma review clinic with a medical professional (GP, respiratory clinician, practice nurse) within the last 12 months (to ensure we exclude other causes of breathlessness)
5. Self-report that asthma symptoms are not well-controlled based on a score > 25 in the self-evaluation of breathing questionnaire [26] despite taking medication. This will be taken to indicate an underlying breathing pattern disorder.
6. Ability to stand without any assistive device for at least 20 minutes (to ensure sufficient capacity to complete the intervention)
7. Speak and understand English sufficiently well to receive the intervention.

Exclusion criteria:

1. Dementia or other major cognitive impairment
2. BMI >32 (as increased subcutaneous fat prevents use of breathing visualisation system)
3. Current smoker or smoked regularly within last 6 months
4. Respiratory comorbidity, including COPD, bronchiectasis, cystic fibrosis, pneumonia
5. Significant breathless from condition such as heart disease, cancer, pulmonary fibrosis
6. Any cardiorespiratory disease that requires medical intervention
7. Unable to cancel or postpone other physiotherapy treatment for breathing pattern disorder (during the period they are involved in the study).
8. Unable to cancel or postpone physiotherapy treatment for musculoskeletal pain (during the period they are involved in the study).

We propose to identify potential participants via six mechanisms

1. Through GP practices
2. Through respiratory clinics (secondary care)
3. Through the Research for the Future patient/Asthma + Lung database
4. Via Social media advert
5. Via Poster
6. Via University of Salford Hub advert

Recruitment through GP practices

We will request that the GP Practices identify patients who have a GP diagnosis of asthma and who have attended an asthma review clinic within the last six months. If possible, we will ask GP practices to screen for other inclusion/exclusion criteria (above). The University of Salford will pay a fee to each GP practice to cover costs associated with searching of medical records. Patients identified as eligible will be sent the participant information sheet and the letter of invitation (see "Letter of invitation") and asked to contact the research team directly if they are interested in taking part. Alternatively, eligible patients will be sent a text message (see "Text invitation"). This text message contains a link to a webpage which provides an overview of the study and a link to the participant information sheet (https://hub.salford.ac.uk/volunteer-for-health-research/2025/02/12/breath/). Embedded within this webpage will be a link to an online form

which volunteers will complete if they are interested in taking part. The questions from this form have been copied to the document "Web screening form". All data submitted via this form is strictly confidential and held on a secure server at the University of Salford. With this latter approach, volunteers are still free to contact the research team directly if they would prefer to be screened over the phone. Note that, with either of the approaches described above, the research team will not have access to patient records. However, the GP practice will provide details of the number of invitations sent out so the research team can estimate recruitment rates for follow-on studies.

Recruitment through respiratory clinics (secondary care)

To recruit through secondary care outpatient clinics, we will follow the same approach as explained above for GP recruitment. Specifically, patients who have consulted for asthma within the last 6 months will be send a letter or text invitation to participate. In addition, eligible patients will also be provided with the participant information sheet during consultation and asked to contact the research team directly if they are interested in taking part.

Recruitment through Research for the Future patient database, Asthma+Lung database or University of Salford database

Research for the future hold a database of patients who experience asthma and who have registered their interest in taking part in research studies. Note that "Research for the Future" is an initiative which is part funded by the Clinical Research Network Greater Manchester (NIHR CRN GM) and the Strategic Clinical Network in Greater Manchester (part of NHS England). See https://www.researchforthefuture.org/ for further details. A similar database is held by the Charity Asthma and Lung (https://www.asthmaandlung.org.uk/). At the University of Salford, we also hold a database of people interested in respiratory research. People registered on these databases who live around the GM area and who have a diagnosis of asthma will be sent the participant information sheet and the invitation letter or sent a text/link to the webpage, described above.

*Recruitment through Social media advert/*University of Salford Hub advert

We will use social medial channels, such as Twitter, Facebook, and Instagram to promote the study (see "Social media advert"). Individuals who are interested in participating in our research will be directed to the webpage described above.

Posters around the University, NHS sites and community settings

We will place poster advertisements (see "Poster BREATH") around the University of Salford and within NHS sites, such as GP practices. We will also put the poster in community sites, such as churches/mosques and shopping centres. The poster contains a QR code, which links to the webpage described above.

Recruitment through University of Salford Hub advert

We will use University of staff internal hub (web page) to promote the study (see "Hub advert"). Individuals who are interested in participating in our research will be directed to the webpage described above.

Identification of physiotherapists

We will reach out to NHS respiratory physiotherapists through professional groups, such as the "Association of Chartered Physiotherapists in Respiratory Care" and through NHS trusts. Specifically, we will send an email (see "Physiotherapist email") around members/staff and attach the physiotherapist participant information sheet. Physiotherapists who are interested in taking part will contact the research team directly.

Strategy to ensure representation across different social/demographic groups

We will take steps to ensure that the sample of participants recruited is representative of the population the study in targeted at. We will assess the diversity of ethnicity and socioeconomic status across each GP practice. This information will then be used to guide choice of GP practices to maximise the likelihood that patients from underrepresented groups will volunteer to participate. Furthermore, as part of our baseline dataset, we will collect data on EDI characteristics, such as ethnicity, sexual orientation and religious beliefs (see description of outcomes below).

4 Consent

With the methods of recruitment described above, patients will either contact the research team directly (via phone or email) or will be provided with information on eligibility via the online screening form. In both situations, participants will have been instructed to read the PIS before either contacting the research team or completing the form. Patients who are deemed ineligible through the screening form will receive a text message or email (depending on preference) to explain that they are unable to take part. Those who appear potentially eligible (after completing the form) or who contact the team directly, will undergo telephone screening to confirm that all inclusion/exclusion criteria are met (see eligibility criteria above).

For those who are eligible, consent will be collected via post in a prepaid envelope marked as confidential or electronically. Specifically, participants will be sent the consent form and asked to return the signed copy via mail or scanned email attachment. Once the consent form has been received, the patient will be formally enrolled onto the study. Any information from patients who do not fulfil the study's criteria will be permanently deleted and only the ineligibility criteria will be recorded. One of the exclusion criteria is a BMI>32. As some participants may not know their weight and height accurately, there will be some leeway on this criterion.

Once enrolled, each patient will be required to complete baseline questionnaires via an electronic form. Note that we will collect the same dataset for patients involved in Stage 1 or Stage 2. Once all baseline data has been received, the intervention coordinator (member of the research team) will liaise with participants to schedule the focus group/interviews (if applicable) and the intervention sessions.

5 The CMT Intervention

Every patient recruited into the study (in both Stage 1 and Stage 2) will receive between 7-8 weekly sessions of CMT at the University of Salford from an experienced NHS respiratory physiotherapist. This physiotherapist will be a member of the research team with experience of delivering the CMT intervention. Each treatment session will last 45-60 mins. The intervention is described below.

Breathing visualisation system:

To support delivery of the treatment, a breathing visualisation system will be used. This system uses two small 3D cameras placed in front and behind the patient. A set of 30-40 small green stickers are placed across the patient's chest/back/abdomen which are monitored by the cameras as the patient breathes. For the system to work, male participants are required to remove clothing from their upper body, however female participants wear a sports bra. A computer program uses the 3D movement data from the stickers to infer the underlying mechanics of breathing, i.e. rib motions and diaphragmatic movements. Breathing patterns are then displayed on a screen in real-time. Although the patient is required to expose their upper body for the breathing visualisation, they can wear a lose fitting t-shirt during most of the treatment session.

In the current study, the breathing visualisation system does not fall within the category of a medical device. The technology used is CE marked equipment (Intel L515 3D camera system) which will not be modified. The system will be used to create a virtual 3D model of the individual which can be presented back using a monitor. This visualisation will only show live movement of the body, enabling individuals to visualise the mechanics of their breathing in real-time. Within the CMT intervention, this visualisation is being used to provide patient education and assist with interoceptive awareness only. The system and software will not provide any calculation of good or bad breathing pattern and no guidance will be given by the system for adjustment of breathing. All decisions on treatment will be made by the physiotherapist and the visualisation of breathing pattern will not, in any way, inform clinical decision making. However, as part of this study we will collect specification data which inform future development of our breathing software as a medical device. This future application would be explored through a different project/ethical approval.

Clinical assessment:

Before the start of the treatment, we will perform a routine clinical assessment in line with the assessment that would be performed on the NHS by a respiratory physiotherapist. If any red flags are identified (e.g. chest pain, unmanage breathlessness unrelated to BPD), the patient will be referred to their GP and the treatment paused until any symptoms are medically managed. During the initial assessment, the physiotherapist will ascertain if the patient is fit to exercise. If not, the treatment will be modified appropriately (see below).

Overview of the intervention

In the text below, we have outlined an implementation of CMT for patients with asthma+BPD. Although this will be adapted throughout study 1, we are confident that the structure of the intervention will remain the same and that our description outlines all the clinical techniques used during intervention delivery.

There are five separate components to the CMT which the physiotherapist works through sequentially. For each component, we will create a clearly delineated protocol which the physiotherapist will follow when they deliver the intervention. The five components are:

CMT Component 1: Understanding asthma and breathing pattern disorder

Animated videos explain the mechanics of breathing and the difference between breathlessness from true asthma (bronchoconstriction) and breathlessness from BPD. Animated videos are used to explain that tensing postural muscles will interfere with the mechanics of breathing and that there can be contexts which are subconsciously associated with muscle tension, and which may therefore trigger breathlessness. After presentation of the theory, the breathing visualisation system is used to help patients understand, and mentally picture, their current breathing pattern.

CMT Component 2: General relaxation

Specific clinical techniques are used to teach patients to release patterns of muscular holding, both in the trunk and in the arms and legs. Guided by instructional videos patients then learn a slow relaxed diaphragmatic breathing pattern in lying and then sitting. They also learn to improve motion at the costovertebral joint (joint between the rib and spine) to improve rib motions and to become aware of tension in the neck and shoulders that might be linked to BPD.

CMT Component 3: Postural deconstruction

The aim of this component is to improve the organisation of postural tone (ongoing low-level muscle activity which supports the body against gravity). This re-education centres on teaching patients to reduce elevated tone in the abdominals and anterior neck muscles, which is triggered by lifestyle and/or

psychological factors. To balance this increase activity and prevent the spine flexing forwards, compensatory activation of the back muscles is required. This leads to a "tug-of-war" between the abdominal and back muscles, with elevated stiffness in the abdominal wall. This increased stiffness prevents a normal breathing pattern, e.g. by blocking the motion of the diaphragm. Using a set of hands-on clinical techniques, the physiotherapist guides the patient to release postural compensation and become aware of, and release, tension at the front of the body. Working against a wall in a standing position, the patient learns to use an integrated breathing pattern (combined diaphragm and rib motions) without triggering any postural compensations. Once they can do this against the wall, they are guided in free standing and in sitting.

CMT Component 4: Contextual triggers

A key principle of CMT is that specific contexts/tasks become associated with subtle increases in tension in postural muscles. Patient are taught to imagine these contexts in a lying position and to become aware of the link between context and muscle tension. Guided by the physiotherapist the patient learns to mentally rehearse specific tasks without triggering the undesired increases in muscle tension.

CMT Component 5: Functional Integration

In the final component, the physiotherapist works with the patients across a range of simulated real-world tasks that can provoke breathing difficulties, such as walking/talking/deskwork. Once the patient can maintain an optimal breathing pattern during activities which require minimal physical exertion, the aim is to gradually increase exertion to more vigorous exercise. To do this, the physiotherapist (supported by the breathing visualisation system) guides very slow deep breathing in standing. The patient then very gradually increases exertion level (either walking on the spot or on an exercise bike) whilst being guided to maintain an optimal breathing pattern. Note that we omit this part of the intervention if the patients is not medically fit to exercise. Following the session, the patient is encouraged to gradually increased their maximal level of exertion over a 2-4-week period but to stop if they experience any breathlessness, dizziness or discomfort.

Delivery of the CMT intervention is supported with animated videos which explain intervention concepts, and which are watched prior to, during and following the clinical sessions. These videos are delivered through an online platform or via a tablet computer which we will provide to patients who do not have an appropriate device. Although novel, the CMT intervention integrates many standard physiotherapy techniques, such as training to encourage diaphragmatic breathing, muscle flexibility testing and postural assessment. It also integrates psychologically informed practice, which is now well-established across the profession. We are not aware of any risks associated with this treatment and have not observed any adverse effects in previous studies of CMT for musculoskeletal pain. However, some people occasionally experience dizziness associated with changes in blood oxygen saturation levels during breathing retraining. The physiotherapists will monitor blood oxygen levels during treatment and continue to check for signs of dizziness which may require the patient to sit or lie down. We have created a dedicated risk assessment for delivery of the CMT intervention which is provided with the ethics application.

At the end of the treatment, the physiotherapist will write to the patient's GP to explain that they have been involved in the study. In this letter, they will summarise the treatment that the patient has received.

6 Intervention development study

6.1 Overview of the intervention development study

This study will begin with focus group work in which we will present intervention principles to users and seek feedback on how best to create a prototype intervention. We will run two focus groups, one with five patients and the other with five physiotherapists. The prototype intervention will then be delivered to the five patients who attended the initial focus group. We will then seek user feedback through a second focus group with the same five patients. Based on this feedback, the intervention will be refined and then delivered to a further five patients. This second group of five patients will be interviewed to understand their experiences of the intervention to map further improvements. Using this feedback, we will further refine and finalise the intervention and user requirements. This process is described in detail below.

6.2 Initial focus groups and creation of prototype intervention

We will run a co-design workshop with five patients. At this workshop, we will present the results of a literature review and suggest how our existing CMT intervention could be adapted for people with asthma+BPD. We will also demonstrate our breathing visualisation system. Through this co-development work, we will gain insight into patient's illness beliefs and behaviours related to their asthma and breathing pattern disorder. The theoretical domain framework [27] will be used to understand the barriers and facilitators of the intervention and establish adaptations that can improve the design/delivery. Through this user consultation, we will also map system specifications and performance criteria for the breathing visualisation system. This workshop will be facilitated using Topic guide 1 (see "Combined topic guides"). Patients will be paid £20 per hour for participating in the focus group.

We will then run a second co-design workshop with the five physiotherapists. This co-design work will allow us to map current practices in respiratory physiotherapy and to understand barriers and facilitators to delivering the proposed intervention within the NHS. This workshop will be facilitated using Topic guide 2 (see "Combined topic guides"). After the completion of both focus groups, we will work with our PPI group, to explore user feedback and identify the key themes which will be integrated into the prototype intervention. We will record and transcribe discussions from both focus groups. Once transcribed, recordings will be deleted, and all data will be anonymised. We will follow this same process for all other focus group/interview work, described later in this protocol. We will pay physiotherapists at their standard rate for participating in the focus group.

Following the process of intervention mapping [28], we will use learning from the co-design workshops and literature review, to map modifiable determinants of behaviour that have the potential to exacerbate breathlessness in people with asthma. For each determinant, we will use psychological theory, drawing on the COM-B model [23] and theory of illness perceptions, to select appropriate behaviour change techniques [29] which could be integrated into one of our five intervention components. This process will be guided by the behaviour change technique ontology [30] which is a standard terminology and comprehensive classification system for the content of behaviour change interventions. With this insight, we will create a prototype CMT intervention for people with asthma+BPD.

6.3 Intervention delivery and clinical outcomes

We will deliver the prototype intervention (see "Section 5") to the five patients who attended the co-design workshop (described above). We will collect questionnaire data on breathlessness from each participant before the start of the intervention and during the week after they the final intervention session. These

data will be collected through an online form (or via postal questionnaire for those without IT access). We will collect data with the following questionnaires (attached to the application):

1. Self-evaluation of breathing questionnaire (validated) [26]
2. Nijmegen questionnaire (validated) [31]
3. Asthma Control questionnaire (validated) [32]
4. Asthma quality of life questionnaire (validated) [33]
5. Generalised Anxiety and Depression Scale (validated) [34]
6. Credibility and expectancy questionnaire (post-intervention only) (validated) [35]
7. Breathing retraining engagement (custom)
8. Healthcare utilization and asthma exacerbations (initial assessment only) (custom)
9. Diversity and inclusion survey (initial assessment only) (custom)

6.4 Mechanistic outcomes

In addition to questionnaire data, each participant will attend for a 30-minute assessment before the first intervention session and for a 30-minute assessment at the end of the final intervention session. During these two assessments, we will measure height, weight and hip-waist ratio. We will also use a heart rate monitor (chest strap) to quantify heart rate and heart rate variability and a sensor (placed on the finger) to measure blood oxygenation level. These measurements will be performed in a lying position. Objective data on respiratory function will also be collected using a desktop spirometry device. This will allow us to quantify lung function, characterising the amount and speed of air flow inhaled/exhaled during normal and deep breathing. In addition, we will use FeNo (fractional exhaled nitric oxide), a simple test to quantify airway inflammation. This is a very quick test which simply requires the participant to blow into a tube.

To characterise breathing mechanics, we will use a 3D camera system. For this measurement, participants will stand between two cameras (see description of the breathing visualisation system, Section 5) whilst they breathe normally for 1-2 minutes. This system allows us to estimate tidal volumes (air flow in/out of the lungs) and to quantify coordination between rib and diaphragm motions. Note that we do not collect digital images with this 3D camera system, and it will not be possible to recognise participants from any of our mechanistic data.

6.5 Collection of data to inform intervention development

We will collect feedback directly after each clinical session from both the patient and physiotherapist through a short interview with a qualitative researcher. In the interviews, we will focus on barriers and facilitators of using the intervention to changing behaviour, and participants will be invited to reflect on our chosen behaviour change techniques. In addition, members of the research team will observe a subset of the clinical sessions directly, noting specific aspects of the clinical protocol which the patients may have found challenging.

6.6 Second focus group and creation of second iteration of the intervention

Once all intervention sessions are complete, we will run a second co-design workshop with the five patients (who received the intervention) to gain further insight into perceptions and experience of the intervention. This workshop will be facilitated using Topic guide 3 (see “Combined topic guides”). Learning from the interviews and the co-design workshop will be recorded and transcribed and presented alongside

observations from the research team and the short interviews (after intervention sessions). We will use thematic analysis [36] and a framework developed to understand the acceptability of healthcare interventions [37]. This analysis will be presented to our PPI group who will work with the research team to map improvements to the intervention. Through this work we will define a second iteration of the CMT intervention for asthma+BPD. Again, we will pay patient £20 per hour for participating in the focus group.

6.7 Intervention delivery to further five patients

The second iteration of the intervention will be delivered to another group of five patients with asthma+BPD. We will repeat the co-design process described above, using short interviews after each clinical session and through direct observation of intervention delivery. These interviews will be facilitated using Topic guide 4 (see "Combined topic guides"). We will also collect questionnaire data (see Section 6.3) along with mechanistic data (see Section 6.4). Following intervention delivery, we will interview each patient to gain insight into barriers and facilitators to using intervention techniques during daily life. These interviews will be carried out over video conference or via telephone (depending on participant preference), transcribed and data anonymised. We will again use thematic analysis to interpret the data and work with our PPI group to map a final set of changes to the intervention. Once implemented, these changes will define the final intervention which will be tested in Stage 2 (pilot study). Patients will be paid £20 for the interview.

7 Pilot study

Each of the 20 participants recruited into the pilot study will receive the final intervention through 7-8 weekly sessions (see Section 5).

7.1 Clinical and mechanistic outcomes

The clinical outcomes (see Section 6.3) will be collected by post or online form at the following time points:

1. Two months pre-intervention (two months before the baseline measurement)
2. Baseline (one week before the start of the intervention)
3. Two weeks post-intervention (two weeks after the final intervention session)
4. Three months post-intervention (three months after the final intervention session)

In addition to the outcomes listed in section 6.3, we will also ask participants whether they feel that they use their reliever inhaler more/less/the same when compared to before the treatment. This question is provided in the document 'Question on inhaler usage' and will be asked at the final two outcome points (two weeks post-intervention and three months post-intervention). We will also collect mechanistic outcomes (see Section 6.4) before the first and after the last clinical session and monitor any adverse events which might occur during the trial.

Process and reminder schedule for the collection of follow-up outcome data (collected after the intervention)

We will send a letter with request for the outcome data at two weeks and three months post intervention, see document 'Questionnaire cover letter'. The research team will monitor outcome, identify missing outcome data and send reminders as appropriate. Reminders for the two-week and three-month (post-intervention) outcome data will follow the schedule below:

- **At 3 days after the initial invitation to complete outcomes is sent**, if outcome data not completed, a Trial Administrator (or the REDCap system) will e-mail the participant with a reminder to complete outcomes.

- **At 1 week after the initial invitation to complete outcomes is sent**, if outcome data not completed, a Trial Administrator (or the REDCap system) will e-mail the participant again with a reminder to complete outcomes. They will also receive a reminder phone call from the research team.
- **At 2 weeks after the initial invitation to complete outcomes is sent**, if outcome data not completed, a trial administrator, will telephone the participant to obtain a minimal data set. This minimal dataset will include the self-evaluation of breathing questionnaire and the Nijmegen questionnaire.

7.2 Sample size and statistical analysis

We will use paired t-tests (or non-parametric equivalent) to explore changes which have resulted from the intervention. With 20 participants, the study will be powered to detect a change of 0.65 SD, power = 0.8 and critical $\alpha = 0.05$. In addition to the formal statistical analysis, we employ a descriptive analysis to inform planning for a future clinical trial. Specifically, outcome data will be summarised descriptively using mean (SD) for parametric variables and percentiles for non-parametric variables. Trial follow-up rates and intervention session attendance will be summarised. We will plot line graphs to look at the trajectory of each outcome over time, looking at both individual participants and the mean values for the whole group.

7.3 Qualitative evaluation

After the final outcomes have been received, we will interview each participant to explore their experiences of the intervention. It will also enable us to gain insight into whether the intervention has been able to help participants manage other comorbidities, e.g. neck pain or gastrointestinal reflux. With each patient, we will explore intervention acceptability through semi-structured interviews performed over the phone or via video conference. Using a conversational style of interviewing, with the questions to direct not to restrict the conversation, we will gain insight into the participants' personal experiences/opinions of the intervention (usability, adherence, effectiveness, and acceptability) and how it contrasts with their previous experience of asthma interventions. The interview questions will relate to the acceptability framework developed by Sekhon et al. [38], after which we will use thematic analysis [39] to identify personal feelings and emotions in relation to patients' experience. These interviews will be facilitated using Topic guide 4 (see "Combined topic guides"). Patients will be paid £20 for the interview.

8 Project timetable

The project will run for 18 months. Stage 1 be delivered over the first 9 months, with the preliminary intervention ready at Month 3 and the final intervention ready at Month 9, following two cycles of iterative co-design. We deliver the intervention to 20 patients and collect outcomes in Months 10-16, with the qualitative analysis carried out in Months 11-14. There will be two months for data analysis after the final outcomes have been collected. During this period, we plan to create an application for follow-on funding.

9 End of Study Definition

The end of the study is defined as return the final (3-month) questionnaire from the final participant in the pilot study (Stage 2).

10 Data Management

In compliance with the University of Salford's regulations, all data and consent forms will be securely maintained throughout the study. Upon its conclusion, consent forms will be disposed of. During the study, consent forms will be stored in a securely locked filing cabinet on university premises. All collected data will remain anonymous. The only link between this number and participant ID will be via the consent form. All data will be transferred from a paper sheet (if appropriate) to electronic files within 1 week of data collection and the original paper copy destroyed.

Interviews will be recorded and transcribed using Microsoft Teams. Once the interview has been transcribed and confirmed as accurate, the recordings will be destroyed. Interviews will be conducted using

a password-protected computer provided by the University of Salford. This device will be stored at the University when not in use.

All electronic data will be safeguarded on a password-protected computer at the University of Salford. Adhering to NHS guidelines, we will retain the research data, which includes experimental and clinical records, as well as opinions on the intervention, for a period of three years, after which it will be destroyed.

Data analysis will be conducted on password-protected University of Salford computers, in accordance with the institution's data management policies. Access to the data will be limited to key research personnel, namely the chief investigator, primary investigator, and the clinical trial coordinator.

11 Dissemination

We will publish a paper reporting on intervention development and pilot testing. We will also publish a paper which will report on user perceptions of the new intervention, as understood through our qualitative evaluation. We will also send each participant a written summary of the research findings and promote the findings through magazine articles.

12 Participant and public involvement

We have formed a user advisory group, consisting of six patient representatives who will advise on research design, participant information resources and dissemination. This group has reviewed the protocol and participant information resources and helped to shape the research. The group will attend regular PPI meetings over the duration of the study.

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