BEhaviour change to reduce Pain in Knee Osteoarthritis (BEPKO-2) – Feasibility study

1. Background and rationale

Knee osteoarthritis (KOA) is a chronic long-term condition which results in pain, disability and reduced quality of life [1]. Estimates suggest that one in three people over 40 will develop knee pain within 12 years [2] and that 10% of the UK population over the age of 55 will be diagnosed with KOA [3]. The NICE-recommended clinical pathway for people with KOA is an initial course of physiotherapist-delivered muscle strengthening [4]. If this fails, then patients proceed to orthopaedic referral for more invasive treatments, including total knee replacement. Before the Covid-19 crisis, approximately 80,000 knee replacements were carried out annually in the UK at an estimated cost of over £500 million[5]. Such numbers, and associated healthcare costs, demonstrate that muscle strengthening does not provide sufficient pain relief for many people with KOA. Furthermore, with the recent cancellation of elective orthopaedic surgery, numbers on waiting lists for knee replacement are growing rapidly. Therefore, there is an urgent need to improve the conservative management of people with KOA who do not respond to muscle strengthening.

While current guidelines focus on the use of exercises to improve strength, there is clear evidence that people with knee OA over activate their muscles during functional tasks [6-8]. This overactivity is characterised by both increased amplitude [9] and prolonged duration [7] of the knee flexor and extensor muscles. Biomechanical research has demonstrated the potentially damaging effects of these patterns, showing that muscle overaction is linked to pain [10], elevated joint load [11] and a more rapid rate of cartilage loss [12]. It is therefore important to understand the potential of conservative management techniques which focus on reducing muscle overactivity.

Psychosocial factors have been linked with clinical pain/disability in knee OA. For example, catastrophising [13] and anxiety [14] have been associated with pain intensity and kinesiophobia linked to physical function [15]. Given these links, a number of physiotherapy interventions have been developed which integrate psychological techniques [16, 17] with muscle retraining. However, these interventions have focused primarily on muscle strength training. Therefore, it is unclear whether improved clinical outcomes would be obtained if psychological techniques were integrated with training to reduce muscle overactivity.

Through a previous NIHR project (BEPKO-1), we developed a new behavioural intervention for people with KOA. This intervention was developed from concepts to central sensitisation to generalised body pain, motor responses to knee pain and also focused on the idea that increased knee muscle overactivity could result from postural compensation. Building on these ideas, the final intervention comprises five components: making sense of pain; general relaxation; postural deconstruction; responding differently to pain; and functional muscle retraining. To facilitate delivery, the intervention incorporates a range of animated instructional videos to communicate concepts related to pain and biomechanical theory and also used EMG biofeedback to facilitate visualisation of muscle patterns. Given the integration of cognitive and muscular techniques, we refer to this new intervention as cognitive muscular therapy (CMT). Preliminary clinical data showed a 69% reduction in pain with very positive user feedback, following six individual sessions of CMT. Given these encouraging findings, further clinical research is required to investigate the clinical efficacy of the CMT intervention.

Current best practice for the first line management of knee osteoarthritis is a group-delivered physiotherapy exercise programme, known as ESCAPE-pain (Enabling Self-Management and Coping of Arthritic Knee Pain Through Exercise). While highly cost-effective, research demonstrates that approximately 40% of patients with KOA fail to experience any clinically meaningful benefit from ESCAPE [18]. Therefore, our proposed study trial will investigate into whether the CMT intervention can provide benefit to people who do not respond to ESCAPE exercise. As such, it will constitute a first step towards the evidence needed for a new pathway for KOA in which patients receive standard exercise physiotherapy first and if they don't experience benefit, would be referred for the CMT intervention before going on for costly orthopaedic referral. The proposed study is a feasibility trial and will inform the design of a future large-scale randomised controlled trial.

2. Overview of the CMT intervention

The CMT intervention is delivered through seven individual 45-60 minute physiotherapy sessions, each separated by a period of two weeks. There are five separate intervention components which the physiotherapist works through sequentially. A summary of each intervention component is provided below:

Component 1: Making sense of pain: This component focuses on patient education, challenging the idea that knee osteoarthritis pain is the inevitable result of "wear and tear". Patients are introduced to the concept that muscle overactivity can increase pain and that brain processing and psychosocial factors can shape the pain experience.

Component 2: General relaxation: Patients are taught to become aware of inappropriate contraction of the quadriceps muscles and to learn a relaxed diaphragmatic breathing by minimising low-level contraction of the abdominal muscles. This component initiates the process of muscular re-education.

Component 3: Postural deconstruction: A set of clinical procedures are used that enable the physiotherapist to unpick (deconstruct) patterns of postural muscle activity and associated patterns of hip/trunk muscle stiffness. Working through the procedures, the patient is provided with experiential learning of how to stand with reduced postural muscle activity and more relaxed knee muscles.

Component 4: Responding differently to pain: This component aims to raise awareness of inappropriate contraction of the knee muscles which can be triggered by pain expectations. Using biofeedback, the patient is taught to minimise anticipatory muscular contraction, which can occur before initiation of movement. Patients are also encouraged to reflect on emotional responses to anticipated pain.

Component 5: Functional muscle retraining: Muscle biofeedback software is used to visualise knee muscle activation during different functional tasks. This software contrasts the patient's muscle patterns with those collected from a healthy group. Using the biofeedback software to guide learning, patients use motor imagery to reduce muscle overactivity, gaining experience of how to perform everyday activities with improved muscle coordination. As part of this learning, the physiotherapist continues to challenge beliefs that certain movements should be avoided.

Delivery of the intervention is supported through the use of 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. EMG biofeedback is also used, in components 2-5, to visualise muscle patterns. This requires the physiotherapist to place small sensors on the skin overlying the patient's knee muscles. Muscle activation data is then visualised on a laptop computer.

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. The key difference with conventional physiotherapy is that the CMT intervention aims to develop awareness of muscle tension, rather than use muscle strengthening. As such, there are negligible risks with this approach, and we did not observe any adverse effects in our intervention development study. Between the clinical sessions, patients are provided with exercises to practice, encouraged to integrate learning into everyday activities and to change the way they think about their knee pain. More information on the CMT intervention is provided in the publication of our intervention development study [19].

3. Feasibility study

This trial will deliver key parameters that are required to run a future, pragmatic, two-arm RCT designed to understand the clinical and cost-effectiveness of the CMT intervention for people who fail to benefit from the NICE-recommended ESCAPE (Enabling Self-Management and Coping of Arthritic Knee Pain Through Exercise) programme or other form of physiotherapy. For this study, we will work with ESCAPE providers to identify people who have received ESCAPE over the previous two years, but not experienced any meaningful clinical improvement in pain. We will recruit 90 patients who will be randomised 1:1 into two groups: an intervention group who receive the CMT intervention, and a control group who will receive advice to continue with ESCAPE exercises. Those in the intervention group will receive seven sessions of CMT over a 13-week period and we will collect outcomes at baseline, 20 weeks and eight months post randomisation (randomisation will happen six weeks before treatment commences). Data will inform planning for a future trial. Full details are provided below.

Unfortunately, all providers stopped delivering the ESCAPE programme during lockdowns of 2021 & 2021. Although many have returned to normal delivery, many ESCAPE services are still paused. Therefore, if recruitment through ESCAPE sites does not allow us to deliver to target, we propose to identify participants through two additional avenues: musculoskeletal clinical assessment and triage services and surgical waiting lists. Details are provided below.

3.1 Recruitment and inclusion

We will recruit 90 patients who have received the ESCAPE group intervention (or other form of physiotherapy) for knee OA over the previous three years but have not experienced an improvement in pain above the minimally important clinical threshold of 15% [18, 20] relative to their pre-treatment state. Patients will be randomised 1:1 into two groups: an intervention group who receive the CMT intervention, and a control group who will receive advice to continue with ESCAPE/physiotherapy exercises. We propose the following inclusion/exclusion criteria which will allow us to identify those who have not benefitted from ESCAPE (or other form of physiotherapy), despite good adherence:

Inclusion criteria

1. Above 40 years old
2. Speak and understand English sufficient to read the information sheet and sign the consent form
3. Ability to walk without any assistive device for at least 100m (to ensure sufficient mobility to complete the intervention)
4. Clinical diagnosis of KOA according to ACR criteria [21]
5. Pain for at least six months' duration

6. Adherence to previous physiotherapy:
    a. Recruited via ESCAPE classes: Attended a minimum of six (of 10/12) ESCAPE pain classes
    b. Recruited via either musculoskeletal clinical assessment and triage services and surgical waiting lists: Attended at least four physiotherapy sessions/classes (typically offered on the NHS)
7. No meaningful benefit from previous physiotherapy:
    a. Recruited via ESCAPE classes: Improvement in KOOS following ESCAPE <15% from their pre-ESCAPE condition [18, 20]
    b. Recruited via either musculoskeletal clinical assessment and triage services and surgical waiting lists: Improvement in self-reported pain <15% from their pre-physiotherapy condition

Exclusion criteria

1. Dementia or other major cognitive impairment.
2. BMI >33 (as increased subcutaneous fat prevents collection of surface EMG signals)
3. Lower limb arthroplasty
4. Any systemic inflammatory disorders, such as rheumatoid arthritis
5. Any balance disorders which may increase the risk of a fall
6. Not fully vaccinated against Covid-19 (for the safety of the physiotherapist and research staff)

As explained above, we propose three methods for identifying potential participants:

1. Through ESCAPE pain providers
2. Through musculoskeletal clinical assessment and triage services
3. Through surgical waiting lists

While our preferred option would be to use only ESCAPE pain providers, we need to include options (2) and (3) above as backup to ensure that we recruit to target. We have summarised each recruitment method below:

Recruitment through ESCAPE pain providers

Many ESCAPE providers collect KOOS outcome data as part of their service. In this scenarios, we will work directly with the ESCAPE provider who will identify individuals who have attended a minimum of six ESCAPE sessions but reported minimal change in the KOOS score. Our initial plan is to recruit incident cases, screening records at the point when patients complete the ESCAPE programme. However, if this does not allow us to achieve our target of 1 participant per month from each ESCAPE site, then we will contact patients retrospectively (who have attended over the previous 6-12 months) to increase the rate of recruitment. With the proposed approach, potentially eligible participants will be sent the participant information sheet (PIS – Feasibility study (patient)) and then asked to contact the research team if they are interested in taking part.

A growing number of ESCAPE providers have switched to a fully anonymised online method of collecting KOOS outcome data. These providers are therefore unable to identify patients who fail to benefit from ESCAPE. In this scenario, we propose to obtain consent from individual patients to collect KOOS data before they enrol onto the ESCAPE programme. In this scenario, ESCAPE providers will provide the letter of invitation (Letter of invitation – collection of ESCAPE outcomes) and the patient information sheet (Participant information sheet - collection of ESCAPE outcomes) to all patients at the point of first contact with ESCAPE. The patient will independently contact the research team if interested in the study. The research team will then check eligibility and take consent via an online form or verbal consent over the

phone. The participant will then complete the KOOS- pain outcome measure (KOOS questionnaire (ESCAPE outcomes)) pre and post ESCAPE- pain programme. This will allow the research team will screen the results to identify potentially eligible patients who report a minimal change in the KOOS- pain score. These patients will then be contacted by the research team, sent the participant information sheet (PIS – Feasibility study (patient)) for the main study and then asked to contact the research team if they are interested in taking part.

Recruitment through musculoskeletal clinical assessment and triage services

The musculoskeletal clinical assessment and triage services (MSKCAT) service is normally offered to patients with knee OA who have tried physiotherapy and experienced no benefit. To recruit via this approach, a clinical research nurse will contact patients who have been diagnosed with knee osteoarthritis by an MSK CATs clinician. This will include all patients with knee OA seen by the MSK CATs clinic within 6 months of the recruitment start date. The patient information sheet (Participant information sheet - feasibility study (patient)) along with the invitation letter (Letter of invitation - feasibility study) will be sent to all potentially eligible patients. The patient will then independently contact the research team if interested in the study. The research team will check eligibility and ask the patients about their improvement in pain after physiotherapy. Those who report minimal improvement in their pain but who can confirm that they attended at least four sessions of physiotherapy will be invited to participate. They will then be sent the participant information sheet (PIS – Feasibility study (patient)) and asked to contact the research team if they are interested in taking part.

Recruitment through surgical waiting lists

If the first two methods do not identify enough potentially eligible participants to meet the studies recruitment target, we will recruit through orthopaedic waiting lists. The orthopaedic administration team will send out the patient information sheet (Participant information sheet - feasibility study (patient)) along with the invitation letter (Letter of invitation - feasibility study) to all potentially eligible patients to all patients diagnosed with knee osteoarthritis who are on the orthopaedic waiting list. We will ensure that we only contact patients who are due to wait at least 1 year for their operation so that there is no possibility that we will interfere with the current care pathway. Again, the patient will independently contact the research team if interested in the study. The research team will then check eligibility for the study. For this recruitment approach, we will require patients to have attended at least 4 sessions of physiotherapy before they were accepted onto the orthopaedic waiting list.

Recruitment of NHS physiotherapists to deliver the treatment

We plan to recruit six Band 6 physiotherapists to deliver the CMT intervention, two at each clinical site. These physiotherapists will be identified through contacts that we have with local NHS trusts. Specifically, we will liaise with the department lead and ask them to send the information sheet (PIS – feasibility study (physiotherapist)) and ask them to contact us directly if they are interested in taking part.

3.2 Consent and randomisation

We will obtain consent from the physiotherapists via post. Specifically, once they have read and are happy with the information sheet and have talked to the research teams about the project, they will print, sign and return the consent form to the research team (Participant consent form – feasibility study (physiotherapist)).

Patients will be required to contact the research team directly after being identify via one of the methods described above. On first contact, the researcher will carry out screening to ensure that inclusion/exclusion criteria are met. For those who are eligible, consent will be collected via post. Specifically, participants will be sent the consent form (Participant consent form – feasibility study(patient)) and asked to return the signed copy via mail or scanned email attachment. Patients will also return a copy of the data access form (Data Access Form) which provides consent for the research team to view previous x-ray data.

Once the consent form has been received, the patient will be formally enrolled onto the study. However, they will not be randomised, into the control or intervention arm, until six weeks before the treatment is due to commence. For some patients this may involve a wait of up to two months between enrolment on the study and randomisation. However, this is necessary in order to coordinate delivery of the intervention.

Randomisation will be stratified by site using variable block sizes, via a central, web-based randomisation system based at the York Trials Unit, University of York. The allocation sequence will be generated by a statistician from York Trials Unit (University of York) not otherwise involved in the recruitment of participants. Once group allocation has been confirmed the intervention coordinator (member of the research team) will liaise with participants to schedule the intervention sessions for those allocated to the intervention group.

3.3 Physiotherapist training course and assessment of intervention fidelity

Each NHS physiotherapist who participates in the trial will receive training to deliver the CMT intervention via an initial online module (approximately 12 hours), followed by two face-to-face one-day workshops. The online module will provide background information and explain how to apply the CMT clinical protocols through illustration with video case studies. The face-to-face one-day workshops will provide the opportunity to practice the intervention on each other and then, if competent, on patients. In order to minimise risk for the patients we will use a competency framework. This assessment has specific criteria that the physiotherapists must satisfy before they are deemed competent to deliver supervised treatment to patients. The physiotherapists will be assessed at the end of the first half (morning) of the workshop. We will then directly observe the physiotherapists working with patients in the afternoon. A further assessment will be completed at the end of the session. The physiotherapists will then be signed off as competent to practise delivering the intervention independently between workshop one and two.

There will be a period of at 1-2 weeks between completing the online modules and the first workshop and a period of at least 4-6 weeks between the first and second workshop. During the period between the two workshops, the physiotherapists will be encouraged to reflect on their learning and apply their newly learned skills in their day-to-day NHS practice. To encourage this reflection, the physiotherapists will be instructed to keep a reflective diary and to use an online platform to share experiences of delivering the intervention.

We will use a quantitative approach to assess intervention fidelity delivered by NHS physiotherapists. For the assessment, we will develop a checklist with 20-30 items, each of which will measure different aspects of the intervention. During the second one-day workshop, the research team will use this checklist to quantify how well the physiotherapist can deliver the intervention. Insight from this assessment will be used to modify the physiotherapist's learning as appropriate

3.4 Interventions and timing

Participants in the control arm will receive advice to continue exercise in line with the ESCAPE programme (or other type of physiotherapy) and to access usual care as they normally would.

We propose to set up a minimum of three sites (Manchester, Liverpool and Bristol) at which we will deliver the CMT intervention. Each site will be located at a physiotherapy outpatient department, a private physiotherapy clinic or a community setting (e.g. community hall) within relatively close proximity to the ESCAPE providers. Participants in the intervention arm will receive a total of seven supervised sessions of the CMT intervention across a 13-week period (see Section 2.4). It is possible that some patients who are included in the intervention arm will be continuing to practice ESCAPE (or other type of physiotherapy) strengthening exercises. Participants will therefore be advised to stop these exercises for the duration of the trial but to continue with low intensity aerobic exercise. A full description of the CMT intervention is provided in Section 2. Each physiotherapist will record the duration of every clinical session and also record the total number of sessions attended (from a maximum of seven).

In order to monitor intervention fidelity, we propose to capture video recordings from all six NHS physiotherapists at different stages along the 6intervention patient journey. These recordings will only be collected from patients who are happy to be recorded. Using the intervention checklist (described above), fidelity will be scored from the video recording by both the PI and by our expert physiotherapist. We anticipate collecting approximately 15-20 recordings in total during the feasibility trial. Recordings will not be shared outside the research teams and once they have been scored then they will be permanently deleted.

In this protocol, we have not described the specific steps we will take to mitigate against the risk of Covid transmission. Instead, we have included a very detailed explanation of our Covid-related procedures in the attached document “AAA Local Covid19 Risk Assessment” This document details a plan of action based on current guidelines (June 2021). This constitutes a worst-case scenario. When the project starts, we propose to continually adjust (potentially relaxing) our Covid measures so that we are in line with appropriate government guidelines e.g., mask wearing, one-way systems). In addition, we will work with each of the separate research sites to ensure we are compliant with their Covid measures.

3.5 Clinical, QoL & health economic outcomes

As this is a feasibility trial, the primary outcomes will relate to the feasibility of conducting a future, fully-powered RCT (recruitment, retention, and intervention adherence rates) and obtaining parameters required to inform its design and conduct, such as the standard deviation of outcome measures that may feed into the sample size calculation.

Clinical and health economic outcomes will be collected by post or online form at the following time points:

1. Baseline (prior to randomisation)
2. 20 weeks post-randomisation (should coincide with the week after the final intervention for intervention participants)
3. Eight months post-randomisation

We will collect clinical data using the following questionnaires (included with the application):

1. WOMAC questionnaire
2. Pain catastrophizing scale
3. Tampa scale of kinesiophobia

4. Generalised Anxiety and Depression Scale

We will collect the following health economic data (included with the application):

1. EQ-5D-5L
2. Health resource utilisation – custom questionnaire
3. Work productivity and activity impairment (WPAI) questionnaire

3.6 Sample size and statistical analysis

This is a feasibility trial and therefore does not have a primary clinical outcome measure to inform a power calculation. Sample sizes of between 24 and 70 have been recommended for feasibility trials to provide a reliable estimate of parameters required to calculate the sample size for a main trial, e.g. standard deviation of continuous outcomes, recruitment and attrition rates [22-24]. We propose to recruit 90 eligible patients to ensure we obtain at least 70 patients in the final analysis, allowing for a 20% attrition rate. If we identify 900 eligible participants, we will be able to estimate a participation rate of 10% to within a 95% confidence interval of ±2%. This sample size should also be sufficient to allow us to identify a subset of patients for the qualitative evaluation who have varied clinical responses to the intervention.

The number of participants screened, consenting and randomised will be presented by site and month. Reasons for non-participation (ineligible or non-consenting) will be summarised where available. Baseline and outcome data will be summarised descriptively by randomised group and overall using mean (SD) for continuous variables and number and percentage for categorical. Trial follow-up rates and intervention session attendance will be summarised. Clinical outcome data analysis will be exploratory in nature and used to plan our future trial. 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 each randomised group.

We will investigate how outcomes from our intervention may compare to surgery through pairwise randomisation, whereby we randomise people once we have two eligible patients (one in each arm). If the participant in the control arm does undergo surgery, this will trigger a follow-up of both members of the pair to obtain outcomes at a specified time-point post-surgery. We will use this feasibility study as a way to test the logistics of pairwise randomisation, which could be implemented in the main trial. We will also monitor numbers that undergo surgery in both arms and use this information when planning any future large-scale trial.

3.7 Health economic analysis

The feasibility of undertaking an economic evaluation of the CMT intervention versus control will be determined. A full cost-effectiveness analysis will not be conducted as part of this feasibility study. The health economics component of the present study will develop an economic evaluation framework, identify the appropriate instruments for collection of relevant health economic data, and consider the feasibility of data collection methods in order to inform the economic evaluation of a future full trial.

The individual patient-level data collected will be used to explore health outcomes (i.e. the EQ-5D-5L), healthcare resource use and costs of the intervention and control groups. Cost and outcome data will be collected at baseline, 20 weeks and 8 months using participant self-completed questionnaires. Health-related quality of life data will be obtained via the EQ-5D-5L [25] to enable the measurement of participants' utility. Estimates of the raw EQ-5D-5L scores will be presented, both overall and by domain, with completion rates also summarised.

An NHS costing perspective will be taken for the analysis. Healthcare utilisation data will be collected and presented for relevant resources used by KOA patients in primary care and the community (i.e. appointments with a GP, nurse, physiotherapist, occupational therapist and other primary/community care healthcare professionals) and the hospital setting (i.e. hospital outpatient attendances, accident and emergency admissions, day case attendances and inpatient admissions). Participants will be asked to record their resource use specifically in relation to KOA. Mean resource use by item will be summarised and completion rates will be presented. Unit costs for the healthcare resources will be sourced from established costing databases, such as NHS Reference Costs [26] and PSSRU Unit Costs of Health and Social Care [27]. Indicative costs of the intervention will be estimated, incorporating the cost of training, delivering the sessions, and the associated materials, versus the control group. The feasibility of capturing data on capacity to work will be investigated, using the work productivity and activity impairment [28] (WPAI) questionnaire, which enables the estimation of productivity loss due to absenteeism and presenteeism. Missing economic data will be inspected to help guide missing data methods for use in a full economic evaluation.

3.8 Mechanistic Outcomes

Using our EMG biofeedback software (used to deliver the CMT intervention), we will quantify changes in muscle activation during a set of functional tasks for all participants who receive the CMT intervention. This will allow us to understand whether EMG patterns return to those characteristic of people without knee pain. All EMG will be collected by the NHS physiotherapists through two additional measurement sessions, one in the week prior to the first intervention and the other the week after the final intervention. In addition, we will collect the same muscle outcome data, at the University of Salford, from a subset of 10 participants in the control arm. This will allow us to understand measurement uncertainty. To ensure uptake of these measurements, we will offer participants in the control arm £20 for each visit to the University. Of those who agree to attend for measurement, we will select 10 individuals at random.

During the two measurement sessions, the physiotherapist/researcher will measure the participant's height and mass and also take a skinfold calliper measurement of fat thickness over the quadriceps muscle. EMG measurements will be obtained by placing small electrodes over the two hamstrings, two quadriceps and two gastrocnemius muscles. Before electrodes are placed, it may be necessary to shave the skin and use an exfoliating cream. Participants will then be instructed to perform a set of everyday activities, including walking, standing up from a chair, stepping down and balancing on one leg whilst EMG data is recorded. Participants may also be instructed to perform some maximal effort contractions, which involve standing on tip toes, and flexing/extending the knee against a fixed resistance. We will also assess hip flexibility, collect some simple balance measurements using a force platform and collect postural and breathing measurements using a 3D camera.

3.9 Qualitative evaluation and process of intervention delivery

Interview will be carried out by an experienced qualitative researcher explore user's experiences of three separate aspects of the study:

1. Explore patient's experience of being involved in the trial
2. Describe patient's perception of the CMT intervention in comparison to ESCAPE (or other type of physiotherapy)
3. Explore physiotherapists experience of intervention delivery

Each interview will be carried out over phone or via video conference. an opening question will start the dialogue "would you tell us about your experience of trial involvement/receiving the intervention/delivering

the intervention". Dependent on responses, further trigger questions will relate to the different intervention components, experiences or an aspect of trial involvement, see below for further details. Responses will be transcribed, and thematic analysis used to inform planning of a future trial as well as minor modifications to the physiotherapist training course. An interview topic guide has been provided as part of this application to illustrate the type of questions that we would use to capture user's experiences (see Interview topic guide)

Patient's experience of trial involvement: We will interview a subset of patients in the treatment arm and patients in the control arm to understand experiences of being involved in the trial. This will allow us to identify any issues which would need to be considered for the follow-on trial, such as willingness to be randomised and appropriateness of outcomes used to capture pain, health-related costs and other psychological factors related to pain. Hence, in order to capture a wide range of experiences and issues we will employ purposive sampling. It is anticipated that six from both groups would be sufficient to achieve this. In addition, we will contact any individuals who decide not to participate in the trial but who indicate that they are happy to be interviewed, to gain insight into the factors that motivated their decision, and use this to inform participant information resources for the follow-on trial.

Patients' perceptions of the CMT intervention: We will purposively select (through pain outcomes) 15 participants from the intervention arm who demonstrate a range of clinical responses. We will ensure that, with our sample of 15 participants, we include at least two to three who have decided to drop out before completing the full seven intervention sessions, in order to gain insight into reasons for non-adherence. 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 experience of the ESCAPE programme (or other type of physiotherapy). The interview questions will relate to the acceptability framework developed by Sekhon et al. [29] , after which we will use thematic data analysis to identify personal feelings and emotions in relation to patients' experience.

Physiotherapist's experience of intervention delivery: We will interview all six NHS physiotherapists after intervention delivery is complete to understand their experience of delivering the intervention. These interviews will take place over the phone or via video conference. We will use the acceptability framework to explore personal opinions of the intervention and to identify any aspects which were deemed difficult to deliver or which the physiotherapist believed to be challenging for the patient to understand.

In addition to the seeking physiotherapists view on the intervention, we will ask each physiotherapist to complete the Normalisation Process Theory Survey (see NoMAD survey). This will allow us to understand how easy it may be to implement the CMT intervention into NHS practice in future.

3.10 Stop-go criteria for the follow-on trial

Learning from this feasibility trial will allow us to understand the feasibility of running a future large-scale randomised controlled trial. The decision to proceed with a future RCT will depend on whether we can achieve the following stop-go criteria:

1. Recruitment: Average participants per ESCAPE provider per month: red<0.5; amber=0.5-0.8; green>0.8.
2. Adherence: Number of participants attending >66% of clinical sessions: red<60%; amber=60-80%; green>80%.
3. Trial retention: Participants providing 8-month outcome data: red<60%; amber=60-80%; green>80%.
4. Acceptability to patients (qualitative evaluation)

5. Feasibility of training NHS physiotherapists to deliver the intervention (qualitative evaluation)

6. Project timetable

This project will be delivered over a 22-month period. During the two months we will identify all ESCAPE providers and begin recruitment in month 2. Physiotherapists will be trained in Months 5-7 and we plan to have a target of n=90 patients recruited, randomised and consented to participate by the end of Month 13. We propose to deliver the CMT interventions across two separate four-month blocks, Wave 1: Month 8-11 and Wave 2: Month 14-16. Each of the six physiotherapists will be required to treat a maximum of four patients in each wave. Following this timetable, we will have delivered the intervention to 45 participants by end month 17, with the qualitative evaluation completed by Month 19. All follow up data will be collected by the end of Month 20, which will allow two months to finalise our application for a follow-on RCT.

7. Dissemination

The primary academic output from this project will be a paper describing the findings of the feasibility trial, which we will submit to Journal Osteoarthritis and Cartilage. In addition, we will publish papers exploring changes in muscle activity which result from the intervention, with the target journal of Gait and Posture along with a paper reporting on our qualitative evaluation of patient experiences.

8. Participant and public involvement in the proposed research

We will form a user advisory group which will consist of four patient representatives who will advise on research design, participant information resources and dissemination. This groups will attend joint PPI/Steering group meetings at the start of the study and every 4-6 months (6 over the course of the project). The user advisory group will be consulted on several different aspects of research design. For example, the appropriateness of specific trigger questions used in the interviews designed to elicit user perspectives of our intervention and on trial involvement.

9. References

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