Project Title

Systematic review and integrated report on the quantitative and qualitative evidence base for behaviour change interventions to promote physical activity in people with intermittent claudication (OPTIMA Project)

Project identifier

NIHR130664

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Disclaimer

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DETAIL RESEARCH PLANS

1. FULL TITLE OF PROJECT

Systematic review and integrated report on the quantitative and qualitative evidence base for behaviOur change interventions to promote Physical acTivity in people with InterMittent clAudication (OPTIMA project).

2. SUMMARY OF RESEARCH

Background: People with intermittent claudication(IC) are 40-45% less physically active compared to their age matched without the disease[1]. Physical inactivity is an independent predictor of disease outcomes and all-cause mortality in people with IC[2], whilst habitual physical activity (PA) can provide long-term health and wellbeing benefits. In the UK NHS, a programme of supervised exercise therapy (SET) is the primary recommended treatment for IC, but access, uptake, and adherence are very low[3]. Traditional supervised exercise programmes (SEP) tend to be short lived, generic, and do not often correspond to improved daily PA[4]. Opportunities for supervised exercise are further limited by the Covid-19 situation and associated social distancing measures especially for people with IC who are considered majorly vulnerable adults. This means that patients may be left wondering how to find alternative ways to stay active and reduce their leg pain. Incorporating behavioural change components to exercise interventions contributes to their effectiveness[5] and support maintenance of PA[6]. However, it is unclear which components (behaviour change techniques (BCTs)), theoretical mechanisms, or contextual features of interventions are linked to intervention effectiveness, and for whom, in people with IC. Understanding these will be important to inform scalable interventions to enhance the effectiveness of exercise therapy and support PA maintenance in IC.

Aim: Synthesise the quantitative and qualitative evidence to inform behaviour change strategies to increase PA and/or support long-term change in PA in people with IC.

Research objectives: The overarching objective is to integrate the quantitative and qualitative evidence base for increasing and maintaining PA in IC by behaviour change interventions, researching concurrently to systematically review:

1. The effectiveness of interventions incorporating behaviour change in increasing and supporting maintenance of PA in people with IC.
2. The association between different BCTs, mechanisms of action and contextual features of the interventions to increases in, and long-term post-intervention maintenance of PA in people with IC.
3. The feasibility and acceptability of interventions containing behavioural change for improving/maintaining PA in people with IC.
4. The feasibility of delivering services using interventions containing behavioural change for improving/maintaining PA. in people with IC.

Design: Two systematic reviews (**SRs**) on behavioural interventions which aim to improve PA for people with IC. (1) **SR1** – randomised (RCTs) and non-randomised controlled trials; Two independent reviewers will identify studies and assess the risk of bias in included studies. We will include studies of adults diagnosed with IC, which assess an intervention incorporating at least one BCT. Although our primary focus is interventions targeting PA improvement and report PA at post intervention and/or at follow up, we will also include studies reporting walking and function, whether or not they report PA behaviour outcome. We will look for BCTs that are overtly reported or otherwise code for them if they aren't overtly reported but identifiable). Analyse the content of the interventions for BCTs, theories and contextual factors, and collect outcome results at short-term post-intervention (<6 months) and long term (≥6 months). Meta-analyses and meta-regressions to estimate intervention effect. (2) **SR2** - qualitative and mixed-methods research on patient/provider experiences with interventions. (3) **SRs 1 and 2** - Utilise state-of-the-art methods drawing on the mixed method synthesis approach and logic model to integrate identified effectiveness outcomes with intervention characteristics including components, mechanisms and contextual factors.

Search strategy: SRs 1 and 2 (no language restrictions, from inception until March 2021): Medline, Embase, Cinahl, Embase, PEDro, Web of Science Psycinfo, Social Science Citation Index for primary studies. We will also search the Cochrane Database of Systematic Reviews (CDSR), the Database of Abstracts of Reviews of Effects (DARE), the Health Technology Assessment Database, Trial Registers (ISRCTN, EU Clinical Trial Register, https://clinicaltrials.gov/) will be searched for ongoing studies. We will also search reference lists of included articles. Study authors will be contacted for detailed descriptions of

intervention and comparator groups, qualitative and process outcomes, and outcome data clarification where details about this are missing from the papers.

Research strategy: We have involved stakeholders in framing the review questions, planning the review, and will work with them in interpreting, disseminating, and translating the review findings. **SR1:** Outcomes are daily PA, clinically assessed walking distances, cardiometabolic risk factors, disease outcomes, quality of life, adverse events; Study quality will be assessed using Cochrane ROB 2(for RCTs) and ROBINS-I(for non-RCTs); Code intervention and comparator components (with Behaviour Change Technique-v1 taxonomy; BCTTv1), contextual futures (using the Template for Intervention Description and Replication classification; TIDieR), and mechanism of action (using the theoretical domain framework; TDF); If appropriate, meta-analyses and (bivariate) mixed-effects meta-regression analyses to synthesise evidence and explore intervention characteristics associated with outcomes. **SR2:** Feasibility and acceptability of interventions including the perspective of participants and providers. We will group together feasibility and acceptability data to provide a tabular summary for narrative synthesis of the included articles, and where possible, quantitative data will be pooled for statistical analyses. We will also code and thematically analyse qualitative and mixed-methods research, and assess the quality of included studies. We will then compare patterns and associations to give broader narrative and interpretative themes. **SRs 1 and 2** will be integrated using a mixed methods research synthesis approach.

Expected outputs of research & dissemination: The findings across both SRs reviews will provide evidence to inform the development of interventions to improve exercise management in people with IC. Future strategies based on the findings will not only support engagement with SEPs and encourage long-term regular PA but will also strengthen evidence-based practice within the UK NHS regarding the clinical-effectiveness of alternative therapies to SEP for people with IC. Findings will be disseminated to a range of stakeholders, including clinicians, people with IC, support groups and commissioners articulating the identified policy, managerial and practice implications of the review using summary briefs, infographics and podcasts, alongside other methods. We will produce a report at the end of the project to guide best practice and to inform clinicians and policy makers. The research findings will be disseminated through at least 2 research papers, conference presentations and workshops.

Timelines: Setting-up & finalising review protocol (prefunding M1-3), studies search & screening (M4-8), data extraction & analysis (M9-20), reporting (M21-27).

3. BACKGROUND AND RATIONALE

Peripheral arterial disease (PAD), a manifestation of cardiovascular disease, is a highly prevalent but underdiagnosed condition which is often sub-optimally treated[7][8]. The most common symptom associated with the early-stage of PAD is IC, defined as a symptom of pain, fatigue, or cramping in the lower limbs muscles, classically in the calf muscle, occurring during mild exertion or exercise, such as walking, which is relieved by a short period of rest[9]. Intermittent claudication is associated with reduced walking capacity, restricted activity levels and mobility, diminished health-related quality of life, social isolation, psychological and economic consequences[10][11]. People with IC have increased cardiovascular-related co-morbidities, and suffer an annual cardiovascular mortality which is 3-4 times greater compared to an age and sex matched non-claudicant population[12]. Without optimal treatment or risk factor modifications, IC can develop increasingly severe symptoms with the development of critical limb ischaemia requiring vascular intervention or amputation.

Current NICE guidelines recommend supervised exercise as the primary treatment for IC, because this is more cost-effective and requires less expertise compared with surgical interventions[13]. However, supervised exercise is not routinely available to the majority of patients across the UK due to issues related to funding, and availability of staffing, facilities and expertise[3]. Where available, challenges such as the time and travel required for regular attendance in addition to patients poor exercise endurance due to claudication pain, multiple comorbidities, lack of motivation to exercise, and poor understanding of the disease (including the need for exercising in spite of pain) lead to low uptake and adherence to supervised exercise[14,15]. Furthermore, the purpose of supervised exercise should be to provide participants with the ability to increase their PA, which is achieved by aiming to increase the capacity of an individual to perform habitual PA. However, traditional SET programmes are mainly focused on improving clinically assessed walking distances (e.g. treadmill test/6-minute walk test) with less attention paid to whether the supervised exercise also promotes an increase in habitual PA and/or long-term daily PA. Habitual PA is associated with symptom improvement, reduction in the risk of cardiovascular events, greater life expectancy, and an improvement in quality of life[13]. Indeed, the problem with SET programmes is that patients often do not change habitual PA and go back to an inactive lifestyle at the end of the supervised exercise. Supervised exercise remains the primary recommendation for IC, but strategies are needed to support habitual PA for patients whether or not they enrol in a SET programme[16].

Informing strategies to encourage an active lifestyle in people with IC has been challenging because interventions to change behaviour such as habitual PA interventions are typically

complex with several poorly described interacting components[17]. The use of BCTs in interventions to support change in habitual PA has been effective in various populations[18][5] but there is limited understanding regarding which interventions may be more or less successful and for whom. People with IC share some common barriers to PA with the general population of older adults and physically inactive adults with other long-term conditions. However, IC also presents uniquely specific challenges for PA. For instance, exercise-induced pain, worsened in environmental terrains that aggravate the leg pain, is one of the most prevalent barriers to PA in people with IC[15]. Therefore, evidence about the effectiveness of BCTs and contextual factors that specifically support PA in people with IC cannot be automatically inferred from the wider population, and our review may help tailor programmes to support engagement in PA among people with IC. This project seeks to address these issues by evaluating the literature concerning the feasibility, acceptability, and effectiveness, of behaviour change interventions to increase and support long-term maintenance of PA in people with IC .

We will utilise a state-of-the-art approach for research syntheses, including **logic models** to simplify the background and rationale, frame the results and inform the discussion and conclusions. We will combine a range of methodological approaches to generate the most informative evidence, namely (a) **quantitative evidence of the effectiveness** of behaviour change interventions aimed at improving and/or maintaining PA in IC; (b) **code and analyse the content of interventions** for BCTs, theoretical components and contexts of intervention and explore associations looking at content of effective interventions; (c) feasibility and acceptability data, from studies examining behaviour change interventions aimed at improving and/or maintaining PA in IC; (d) **integrating findings from quantitative and qualitative evidence** using a **mixed methods research synthesis approach.**

3.1 Burden of disease

Peripheral arterial disease affects more than 3 million people in the UK NHS[19], and 1 in 5 people aged over 60 years have some degree of the disease[20]. About 40 to 75% of people with PAD experience the symptom of IC[9], making it one of the main indications for referral to vascular surgeons in the UK. There is inequality in the prevalence of IC as patients are more likely to have finished education on leaving school, have a below median income, and be currently unemployed[21]. Similarly people with IC have a greater comorbidity burden, and are more likely to be obese, to currently smoke and currently consume alcohol[22].

Disease progression and increased disease risk

Intermittent claudication is a chronic condition where pain limits walking, which results in disability due to ambulatory dysfunction[23] and progressive impairment in physical function[11,24]. Without effective treatment the natural progression is to chronic pain in the legs and eventually to non-healing wounds, gangrene and limb loss[25]. Due to the diffuse nature of atherosclerosis and the involvement of other arterial beds, people with IC have a 5.9 times greater risk of cardiovascular disease mortality[26][27] and 3-4 times increased all-cause mortality risk compared to those without the disease[27]. Approximately 25% of people with IC die from coronary or cerebrovascular events within 5 years of diagnosis[12][28], and the overall 5-year mortality is about 33.2%[29]. Compared with people without the condition, people with IC have greater decrements in health-related quality of life[10][27].

Increased costs from severe disease

Intermittent claudication causes significant costs to patients and the NHS, in terms of reduced quality of life, loss of healthy life-years and medical and surgical treatment[30][22]. People with IC have significantly lower health utilities and lower mental and physical component summary QoL scores[22]. Progression of IC can result in worsening symptoms including critical limb ischaemia. The yearly cost to the NHS to treat the 500-1,000 new cases of critical limb ischaemia per million of the UK population diagnosed each year is estimated at £200 million[30]. Compared to non-claudicants, people with IC who are employed report significantly greater levels of absenteeism, presenteeism, and overall work impairment[22]. The number of physician visits, hospitalisations and number of emergency room visits within the past six months are significantly higher in IC compared to age-matched controls[22]. Given the sub-optimal treatment of IC and the ageing UK population, the burden of multimorbid IC patients with multiple significant vascular problems to the NHS is expected to rise over the next decades[31].

Benefits from increasing and maintaining habitual physical activity in IC

Evidence including from systematic review and analysis of two large cohort studies show that individuals with PAD are generally less physically active than those without the disease[32]. People with symptoms of IC are 40-45% less physically active compared to age-matched non-claudicants[1]. Physical inactivity is an independent predictor of disease outcomes and all-cause mortality in people with IC[2]. Increasing and maintaining a physically active lifestyle provides improvement in claudication symptoms, cardiovascular risk factors, overall health and quality of life in people with IC[33].

3.2 Existing reviews

One systematic review in 2013 investigated behavioural techniques for increasing walking in people with IC[34]. The review identified behavioural change techniques (BCTs) associated with increased PA, including self-monitoring, providing feedback on walking performance, and helping patients to identify barriers to walking and solutions to overcoming them. The review was based on a less extensive behavioural change framework, which limited the ability to code the full range of available BCTs present within the current and most comprehensive behaviour change taxonomy (BCTTv1) [35]. It did not utilise any framework to identify the theories present within interventions, in order to appropriately link BCTs to mechanisms of action, when evaluating and reporting interventions or use findings to inform strategies to increase habitual PA. In addition, the review did not examine the possible influence of contextual features of interventions which have implications for designing, replicating or scaling interventions based on the review outcomes. Therefore, not much is known about the intervention components, mechanisms, and contexts that might support increased and/or promote long-term PA behaviour change in people with IC.

With the BCTTv1, reviewers are now able to comprehensively identify the 'active ingredients' (BCTs) associated with the most successful complex interventions. Similarly, it is also possible to precisely code the key causal mechanisms (known as theoretical domains) underpinning behavioural change using frameworks such as the Theoretical Domains Framework (TDF)[36]. In addition, the contextual features of interventions (such as mode of delivery) which may impact intervention effectiveness and which the BCT taxonomy and the TDF do not capture, can now be accounted for using the Template for Intervention Description and Replication (TIDieR) framework[37]. The NICE recommended SET programmes are underutilised in the UK NHS, and effects that can be gained are typically short-term, likely due to inadequate individualisation of the exercise programme with little or no attention paid to supporting long-term exercise adherence. Therefore, identifying both intervention components, mechanism of action and intervention context and their association with an increase in and maintenance of PA behaviour is essential to inform strategies to support patients' short- and long-term improvement in PA. This strategy has the potential to strengthen evidence based practice within the UK NHS regarding the clinical-effectiveness of alternative or adjunct therapies to SEP for patients with IC.

3.3 Why this research is needed now

This systematic review addresses an unmet area of need in a clinically important condition. Chronic symptoms of walking limiting pain, known as IC, is one of the main indications for referral to vascular surgeons in the UK. Current NICE guidelines recommend that all persons with IC receive supervised exercise as a first line management[13]. However, lack of funding means that programmes continue to be unavailable to the majority of patients in the UK NHS[3][38], and widespread implementation is restricted by lack of facilities[39]. Where supervised exercise is available, patient uptake and adherence to programmes remain low, whilst drop out continues to be high [3][38]. In addition, people with IC are more likely to be obese older adults, with comorbidities (e.g. ischaemic heart disease with or without myocardial infarction, diabetes mellitus), on prescriptions for five or more medications (polypharmacy)[40]. This often warrants individual tailoring of exercise to gain patients engagement with programmes for patients to derive optimum benefits. Furthermore, maintaining improved PA is important, as the benefits accrued from supervised exercises are only maintained if patients continue to be active.

Many studies have shown that patients do better if they embrace life-style changes and increase PA in a conservative treatment[41]. As IC already poses an enormous clinical burden, innovative strategies to obtain the patients' co-operation in PA lifestyle changes are an increasingly important component of management[42]. Regardless of whether a patient is undergoing supervised exercise, home-based exercise or is listed for surgery, increasing PA in IC is particularly important for symptom management, disease prognosis, cardiovascular outcomes and health-related quality of life. Where supervised exercise is not available, current NICE guidelines recommend suggesting unsupervised exercise (taking into account patient's motivation and comorbidities) and to advise patients to exercise for approximately 30 minutes 3-5 times per week, walking until the onset of symptoms[13]. However, in addition to challenges that are common to older adults or people with long-term conditions, claudication pain presents additional unique challenges to walking and exercise in people with IC[15]. In addition, the COVID-19 outbreak, characterised by extraordinary measures to prevent the spread of the disease and to re-organise dedicated clinical services, potentially leads to closure of supervised exercise services and less access to opportunities for PA for people with IC who appear to be at greater risk of infection. The future of COVID-19 is still uncertain but even in the event of return to full services, there is a need to orient exercise rehabilitation services and to adjust processes and outcomes to the COVID-19 environment. There is no guidance from NICE on behavioural change techniques specific to IC, particularly informing strategy to encourage uptake and maintenance of PA either supervised or unsupervised. Identifying and specifying the fine-grain detail of the active components of interventions, and

contextual features, in addition to user experiences, will be essential for implementing, replicating and synthesising successful approaches[35]. This review will identify the active ingredients and contextual features that need to be included in person centred interventions to target uptake and maintenance of PA in patients with IC.

3.4 How the intervention might work

A number of studies using various types BCTs to increase physical activity in people with intermittent claudication have been conducted; many of these studies support incorporating BCTs to increase clinically assessed walking distances and suggest that incorporating BCTs in interventions might be beneficial for increasing and maintain daily PA for people with IC[34]. There is good quality evidence which has demonstrated that BCTs supplementary to exercise prescription improved walking ability and increased daily PA of people with IC[6]. Some of the underlying mechanisms through which BCTs may affect benefits include enhanced understanding of disease pathology and the benefit of exercising in spite of pain, enhanced motivation to exercise, and enhanced patient self-management skills[34].

SEPs are the current best practice *treatment* for people with IC, because they are more cost-effective and require less expertise compared with surgical interventions. However, SEPs are not routinely available to all patients across the UK due issue related to funding, staffing, facilities and expertise[3]. Even when available, one of the challenges to implementing SEPs for IC is the time and travel required for regular attendance. In contrast, behaviour change interventions that promote self-managed exercise offer a potentially promising alternative. Such programmes have the potential to improve exercise behaviour at a much lower cost compared to medically supervised programmes. This may also be more acceptable to patients because travel requirements and time constraints are minimised. Such behaviour change interventions could be used to support engagement and adherence to SEPs and encourage long-term habitual PA at the end of SEP (where SEP is available), or encourage habitual PA uptake and maintenance by those who cannot access or engage with SEP.

The information generated from this review will form an important step to the understanding of programme components and contextual features that successfully promote long-term behaviour change to support habitual PA in these patients. Such information will be fundamental in the design of future interventions, whether provided alongside SEP to promote translation of improved walking capacity to habitual PA after the SEP, or as part of a separate behaviour change intervention.

We will follow the staged approach to produce both system-based and process-oriented logic models to simplify the understanding of this review. The *system-based logic model* will be used to conceptualise the objectives, unpack the interventions and consider contextual factors, whilst the *process-orientated logic model* will be used to illustrate how the interventions worked to influence various outcomes and to identify gaps in the evidence base. Drawing on the staged approach, we have created an initial (Version 1) logic model (See figure 1 at the end of document) to populate a system-based logic model template for the HTA questions:

i) In people with IC, can behavioural change interventions deliver an increase in or support long-term change in, PA?

ii) Which BCTs, theoretical mechanisms, and contextual features of interventions are associated with an increase in, or support long-term change in, PA?

iii) What is the feasibility and acceptability of interventions containing behavioural change for improving/maintaining PA in people with IC and the feasibility of delivering services?

The initial system-based logic model drew on the research team's knowledge and understanding of exercise in IC, and a combination of team discussions, method and topic specific literature identified through non-systematic searches[34][15][14][18] and input from patients and clinical members of our Advisory Group. The system components are organised within columns and boxes including Population, Intervention, Intervention design, Intervention delivery, Theory, Outcomes and Contexts. These are then populated with specific information which could influence the effectiveness of interventions.

We will modify this model at various stages of the review namely:

i) Version 2 based on the results of the quantitative review results of effectiveness, and the association between different BCTs and, mechanisms of action;

ii) Version 3 based on the results from feasibility and acceptability data; and iii) Version 4 (final logic model) based on the feasibility of delivering services within the NHS, any additional findings generated through an assessment of context and implementation as well as consultation with stakeholders.

4. PLANNED INVESTIGATION

4.1 Aim

The aim is to synthesise quantitative and qualitative evidence to inform behaviour change strategies to increase PA and/or support long-term maintenance of PA in people with IC.

4.2 Research objectives

The overarching objective is to integrate the quantitative and qualitative evidence base for increasing and maintaining PA in IC by behaviour change interventions, researching concurrently to systematically review:

1. The effectiveness of interventions incorporating behaviour change in increasing and supporting maintenance of PA in people with IC.
2. The association between different BCTs, mechanisms of action and contextual features of the interventions to increase and maintenance of post-intervention change in PA in people with IC.
3. The feasibility and acceptability of interventions containing behavioural change for improving/maintaining PA in people with IC.
4. The feasibility of delivering services using interventions containing behavioural change for improving/maintaining PA in people with IC.

Project deliverables will include: 1) Systematic review and integrative report, including a flow chart format which will include the analysis of the intervention components and contextual features and a final logic model, 2) Funding report, 3) At least 2 journal publications, 4) At least 2 conference presentations, 5) Accessible project newsletters, 6) Key findings document for clinicians, commissioners, policy makers and patients, disseminated via traditional and social media.

4.3 Research plan/Methods

The conduct and reporting of this review will be informed by the Guidance from the Centre for Reviews and Dissemination[43] and the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA)[44]. The conduct and reporting of patient and public involvement in this review will be guided by the ACTIVE framework for stakeholders involvement in systematic reviews[45] and the GRIPP2 guidance for reporting patient and public involvement in health and social care research[46]. This review is registered in PROSPERO (Registration Number: CRD42020159869).

4.31 Design

1. **Systematic review 1** Systematic review of RCTs and non-RCTs of interventions containing behavioural change techniques for short- and long-term change in PA for adults with IC, in any setting. Classification of behaviour change techniques and theories and TIDieR components used in intervention and comparison groups. Meta-analysis for effectiveness and meta-regression analysis to look for features of more effective interventions.

2. **Systematic review 2** Systematic review of feasibility and acceptability including qualitative and mixed-methods research exploring adults' experiences of living with IC and receiving interventions containing behavioural change techniques for PA, any setting, (including research exploring the views of professionals involved in their care).

3. **Integration of findings** in a mixed-methods synthesis to produce a detailed summary of the effectiveness, feasibility and acceptability of interventions containing behavioural change techniques for PA for adults with IC, to understand how the content and processes of the interventions affect participant behaviour to achieve outcomes.

4.32 Health technologies being assessed

Technologies to be reviewed are behavioural and functional (e.g. physical activity, lifestyle, behaviour change techniques, walking capacity, quality of life or combinations of these). Interventions which include innovative mechanisms for delivering services, e.g. web-based/email/mobile phone support will be included.

4.33 Search strategy

We will use a comprehensive search strategy of index free text terms and synonyms located in the title or abstract and representing three broad concepts reflecting the disease (e.g. IC, PAD), behavioural change interventions (e.g. structured exercise, physical activity, lifestyle intervention, motivation, cognitive behavioural intervention) and outcome (e.g. physical activity, exercise) to search relevant electronic databases. We will implement separate searches for **SR1** and **SR2** with no language restriction applied. Our scoping search has identified around 25 RCTs and non-RCTs potentially eligible to evaluate for **SR1** and around 13 qualitative and mixed method studies for **SR2**. As per our scoping searches, we will update this search in at least six databases (CINAHL, EMBASE, Medline, PsychINFO, PEDro, and Web of Science, Scopus until March 2021). We will also search the Cochrane Databases, the Database of Abstracts of Reviews of Effects (DARE), the Health Technology Assessment

Database, Trial Registers (ISRCTN, EU Clinical Trial Register, https://clinicaltrials.gov/) for ongoing studies and will search reference lists of included studied. We will further contact experts in the field to request information on relevant studies not already identified by the aforementioned strategies. Where required, we will contact authors of included studies by email to request full intervention materials/protocols for active and comparator groups (including usual care, or their augmented version), detailed behaviour change technique coding, qualitative and process outcomes, including written reports of any qualitative research and process evaluations.

4.34 Quantitative review methodology – Systematic reviews 1

Inclusion and exclusion criteria

Study design: Reports of interventions using behavioural change techniques and aiming to increase PA in people with IC, any study design with intervention and a comparator arm; pre-post study designs without a separate comparator arm but which compared baseline values to post-intervention values; as well as service improvement evaluations will also be considered in order to include and evaluate as much relevant research as possible. The definition of maintenance in physical activity varies in literature, and various reviews of maintenance outcomes have not specified a minimum post-intervention follow-up period[47][48]. However, maintenance is hypothesised to occur at a minimum of 6 months after initial change[49]. Therefore, we will define maintenance as those assessed at least 6 months post-intervention, and will include any study with a follow-up of ≥ 6months to assess long-term maintenance of PA. However, the review aims to assess both increase and maintenance of PA, and therefore we will also include studies with follow up <6 months in order to assess short-term increases in PA.

Participants: Studies must include only adults (≥ 18 years) clinically diagnosed with PAD and IC.

Interventions: We will include interventions which contain at least one BCT and which aim to assist people with IC to achieve increase and/or maintenance of habitual PA. Our approach towards inclusion of intervention studies is pragmatic. We will include both interventions that are psychologically/educational based behavioural interventions and those which implement active monitoring e.g. using a pedometer, so long as the components used in the intervention can be successfully coded as BCTs. Therefore, interventions in the form of, but not limited to, structured exercise/physical activity, lifestyle, motivational counselling, structured home-

based exercises, comprehensive rehabilitation, structured patient education or combinations of any of these will be included. Studies reporting on any mode of SEP would be eligible for selection if it included at least 1 BCT. We will include different approaches for delivering services, e.g. web-based/email/mobile phone support. Studies examining the type of personnel, frequency of contact, mode of delivery (e.g. group versus individual), use of incentives, or evaluation trials using hybrid implementation science approaches will also be included. We will include studies whether or not change in habitual PA and/or maintenance of habitual PA is explicitly stated as the outcome of the studies. Comparators will be alternative interventions, control interventions or post-intervention versus baseline values. We are aware that there may be a difference in context, for example in terms of required cost, time and staff input, to implement different types of BCT and we intend to comment on possible cost implications of BCTS in our integrated findings.

Setting: All settings for interventions will be reviewed, including hospital, primary care, community settings, home-based voluntary sector, leisure centres or gyms, and digital domains (e.g. mobile telephone apps).

Outcomes: Given that our patient PPI members felt that if secondary outcomes of physical capacity, quality of life and other patient centred outcomes have improved, these are important for people with IC, not just whether physical activity was measured in intervention, we deliberately set our search strategy broadly to capture both primary and secondary outcomes so we will also include studies with secondary outcomes even when PA behaviour is not assessed or reported. To be included, studies must report at least one of the review outcomes at post-intervention as a primary or secondary outcome measure. For PA behaviour analysis, studies must report at least one valid PA outcome (e.g., self-report, activity monitor). It is important to distinguish between initial behaviour change and behaviour change maintenance, which is reportedly more difficult to achieve[50]. We will assess change in habitual PA as those outcomes reported at a period within <6months post-intervention), and long-term maintenance of PA as those outcomes reported at ≥ 6 months post-intervention. Where assessment was taken at more than one time point within <6-month post-intervention, we will record the earliest measurement as the change outcome for the primary analysis. Similarly, where intervention record changes at more than one-time point within ≥6-month post-intervention, we will record the latest measurement as the long-term maintenance outcome. Other quantitative outcomes to be reported include changes in clinically assessed maximum walking distance (MWD) or time (MWT), pain-free walking distance (PWD) or time (PWT), self-reported functional status, health-related quality of life, psychological wellbeing, cardiovascular events, disease

progression including indications for vascular intervention, mortality, and cardiovascular risk markers. Furthermore, data on process outcomes and cost evaluations will be collected[51].

Data collection and analysis

Selection process: Titles identified in the electronic database searches will be exported into Covidence, an electronic tool for managing papers identified in a systematic review. Two researchers will independently screen each title and abstract of the search results followed by screening of full texts of potentially relevant studies against the inclusion criteria. Disagreements at any stage of the screening will be resolved by discussion and reaching consensus or a third researcher will mediate. A PRISMA (Preferred Reporting Items for Systematic Reviews and Meta Analyses) flow chart will be used to present search hit returns, studies screening and selection processes.

Data extraction: To ensure comprehensive data capture, two researchers will develop, pilot and iteratively refine the data extraction forms ('characteristics of included studies' tables) to capture study details and outcome data. This will include author/s, country of study, study design, sample size, population studied (e.g. newly diagnosed, prior intervention), gender, age, comorbidities, ethnicity and level of education), intervention type (i.e. PA only or lifestyle intervention that was not restricted to PA), setting, study duration, attrition rate, outcomes, Behaviour Change Techniques (BCTs) and intervention theories and TIDIER elements. In addition, we will describe funding information and conflicts of interest of authors for all studies in the characteristics of included studies' table. Discrepancies in data extraction will be resolved by discussions and consultation with a third researcher.

Risk of bias assessment: Two researchers will assess the risk of bias in the included studies and discrepancies will be resolved via discussion and consultation with a third researcher if required. The Cochrane Collaboration's Risk-Of-Bias 2 (ROB 2) tool [52] will be used to assess risk of bias in randomised control trials. Risk of bias will be described as 'low', 'high' or 'unclear'. The Risk Of Bias In Non-Randomised Studies - of Interventions (ROBINS-I)[53] will be used to assess risk of bias in non-randomised controlled trials. Differences in opinion will be resolved by consensus or in consultation with a third member of the team, if required.

Identifying behaviour change techniques within the studies: Two researchers will use the Behaviour Change Technique Taxonomy (BCTTv1)[35] to independently code active intervention content based on information presented in the included studies, as well as any associated published protocol papers and/or intervention manuals. We will also collect this

data for the comparator group interventions. We will contact authors for full details of interventions in all study arms where required. Discrepancies will be resolved through discussion and reaching consensus in consultation with a third researcher.

Identifying theoretical causal mechanisms within the studies: Two researchers will independently use the Theoretical Domains Framework (TDF)[36] to code for theoretical content in interventions and control conditions containing psychological or behavioural interventions. TDF integrates key theoretical domains known to be important in understanding behaviour change across a range of populations and health conditions. The TDF contains 14 domains examining, for example, knowledge, skills, social influences and environmental factors that can all influence behaviour. It provides a coherent way of organising explanations of why things do, or do not happen, in relation to theories of behaviour change. In this way the TDF enables insights into potential mechanisms of action for developing or optimising interventions. Discrepancies between coders will be resolved through discussion and reaching consensus in consultation with a third researcher.

Process of identifying theory and BCTs within studies: Verbatim descriptions of the intervention and control/comparator descriptions will be extracted from the identified papers. or companion materials. Two reviewers will independently code intervention theory using the 14 domains of the TDF, and the BCTs with the BCTTv1. Each of the 93 BCTs within the BCTTv1 will be considered for its presence within each intervention description and BCT guidelines will direct the coding process. For all coding, the coders will use a data extraction form, with the coding supported by evidence from the text. Any discrepancies across coders will be discussed with a third coder to reach consensus.

Information to be extracted on theory/BCTs: The following information on theory and BCTs will be extracted from the interventions and control/comparator conditions: i) BCT table of the positive or negative presence of all 93 BCTs; ii) The total, mean number, standard deviation and percentage use of BCTs reported in each study; iii) The percentage use of each of the 16 hierarchical groups within the BCTTv1; iv) Total number and percentage of studies that had a theoretical basis, and the theoretical TDF domains present in the studies.

Identifying contextual features and information to be extracted from the interventions within the studies: We will use the TIDieR framework to guide data collection on the content, context and intensity of the interventions delivered[37]. TIDieR is a general taxonomy for reporting characteristics of any type of interventions and covers many aspects of context which are important for implementing interventions within the UK healthcare setting,

therefore it is well-suited for this review. Using the TIDieR framework, 14 components will be coded for each intervention: 12 components corresponding to each of the items of the TIDieR checklist[37], plus one item to code 'WHO RECEIVED' the intervention (newly diagnosed vs ongoing) and one item to code the type of outcome measure (self-report versus objective measures). Two researchers will independently code the intervention context and discrepancies will be resolved through discussion and reaching consensus in consultation with a third reviewer.

Statistical Methods

Outcomes prioritisation: We will assess increases and maintenance in habitual PA as the primary outcomes and will synthesise objective measurements of PA (e.g. body-worn sensors such as pedometers or accelerometers) separate from self-report measures (e.g. questionnaires). The following will be assessed as secondary outcomes: changes in clinically assessed maximum walking distance (MWD) or time (MWT), pain-free walking distance (PWD) or time (PWT), self-reported functional status, health-related quality of life, psychological wellbeing, cardiovascular events, disease progression, and mortality. We will also evaluate other outcomes such as cost data and process outcome data.

Time points

We will carry out synthesis of data at the following time points:

- Short term: earliest change outcomes assessed within <6 months post intervention
- Long term: latest change outcomes assessed from 6 months post intervention as maintenance of PA [49].

Pairwise meta-analysis

Important clinical and methodological characteristics of included studies will be summarised and tabulated prior to data synthesis. Meta-analyses of pairwise comparisons for primary and secondary outcomes will be carried out where direct evidence is available. Pooled effect sizes, confidence intervals and prediction intervals will be estimated using data from individual arms of included trials. Risk ratios (RR) and risk differences (RD) will be estimated for binary outcomes and mean differences for continuous outcomes (or standardised mean differences using Hedge's g effect size if multiple measures have been used for the same outcome). A forest plot will be presented for each analysis. Stata v13 (College Station, TX) will be used for meta-analyses.

Included studies

Our primary analyses will strictly include evidence from randomised trials. Complex trial designs (multi-arm, cluster and crossover) will be meta-analysed appropriately, in accordance with guidance set out in the Cochrane Handbook [52]. We will conduct additional analyses which will allow the inclusion of non-randomised studies.

Missing data

For all outcomes, analyses will be carried out, as far as possible, on an intention-to-treat basis. For each study, we will extract outcomes as complete case data and baseline observation carried forward (BOCF) data reporting the mean, standard deviations (SD) and number of participants contributing valid data. Where SDs are not presented we will calculate them from 95% confidence intervals, standard errors (SEs) or other statistics which allows the SD to be derived. If BOCF data are not presented we will calculate these values from completer data. We will classify multiple imputed data as similar to completer data because it is primarily based on the outcomes of people that were followed up. In a few cases, some useful data will be missing that would allow us to calculate the mean change in PA, SD, or know the number followed up and we will endeavour to contact study authors to seek such missing data. When data items remain unknown, we will make reasonable assumptions to calculate these data and note these assumptions in the evidence tables. Sensitivity analyses of primary outcome data will be conducted to test these assumptions.

Heterogeneity

A previous review of behaviour change trials in intermittent claudication showed considerable heterogeneity [34]. Heterogeneity will be assessed by visually inspecting forest plots. We will also assess statistical heterogeneity in each pairwise meta-analysis using the I^2, T^2, and Chi^2 statistics [52]. For example, the I^2 statistic quantifies inconsistency across trials and describes the percentage of variability in effect estimates that may be due to heterogeneity rather than sampling error. Heterogeneity will be regarded as substantial where T^2 is greater than zero and either I^2 is greater than 50% or there is a low p-value (less than 0.10) in the Chi^2 test. If substantial heterogeneity is detected, we will explore the possible causes (for example, differences in study design, participants, interventions, or completeness of outcome assessments) in subgroup and sensitivity analyses. We will use random-effects meta-analysis for combining data where significant statistical heterogeneity is present.

Subgroup analyses

If data are available, we will explore whether the effectiveness of interventions differs according to whether all/majority of participants are selected on the basis of newly diagnosed or long-standing intermittent claudication (with or without previous revascularisation surgery). If sufficient data are available, we will also explore the effect of BMI category, comorbidities related to intermittent claudication, sex, deprivation, age, and ethnicity.

Network meta-analysis

We will conduct network meta-analysis so that indirect effect estimates can also be estimated. Network plots will be created to summarise direct evidence. We plan to combine direct and indirect evidence using network meta-analysis (NMA) to estimate treatment effects between all interventions, even where no head-to-head trials have been conducted. The transitivity assumption underlying NMAs will be examined by comparing distributions of potential effect modifiers and, if the assumption is not violated, then NMAs will be conducted for all outcomes subject to sufficient data being available. A frequentist approach to NMA will be undertaken with random effects models fitted with single heterogeneity parameters. Sensitivity analyses will be considered to examine the effect of different classifications of intervention doses or modalities. Interventions will be ranked in order of the probability of being the most effective treatment using surface under the cumulative ranking curves (SUCRAs). Heterogeneity and inconsistency will be examined using I^2 statistics, with node-splitting and inconsistency models fitted to address inconsistency if required. Reporting bias will be explored using comparison adjusted funnel plots. The quality of the evidence from the NMA will be assessed based on the GRADE approach[54] using the CINeMA web application (www.cinema.ispm.ch). Guidelines recommended in the PRISMA extension statement for network meta-analyses [55] will be followed when reporting the NMA.

If neither a pairwise nor a network meta-analysis is possible, then a narrative synthesis will be provided, similar to what was conducted in a previous review of physical activity [56]. Any narrative synthesis will be reported according to recently published SWiM guidelines [57].

Moderator analysis

If sufficient data allow, we will examine contextual factors associated with interventions using mixed-effects meta-regression to explain variation in intervention effect size. We will explore the impact of the following moderator variables: intensity (frequency and duration of sessions);

sample characteristics (including particular inclusion/exclusion criteria); mode of delivery (face to face, group, web, apps, etc); setting (clinical, home-based, etc); adherence to the treatment and fidelity of intervention delivery.

Potential moderators will be fitted separately as fixed effects. A single residual heterogeneity parameter will be estimated using the Knapp-Hartung method [58] and included as a random effect. Regression coefficients will be reported along with the associated p-value from z-tests of significance. Model fit will be examined with likelihood-ratio tests.

Behaviour change techniques and contextual factors (TIDieR elements) associated with intervention effects

We will identify which combinations/clusters of BCTs and delivery/context features such as those from the TIDieR checklist are associated with effectiveness using the meta-CART analysis replicating the methodology used in a recently published systematic review to assess associations with cluster of BCTs and TIDIER elements with increased healthy behaviour in randomised controlled trials (RCTs) for low-income adults [59]. Meta-Cart combines meta-analysis with recursive partitioning (specifically Classification and Regression Tree methods) to estimate interaction effects between moderators and thus identify effective combinations of interventions [60]. The regression tree will be built using moderators previously identified as being significant, with splits in the tree defined when between-group heterogeneity is maximised. Subsequent pruning of the tree will be conducted by removing splits based on cross-validation errors in order to identify any synergistic effect between moderators. The extent to which the synergistic effect explains heterogeneity between interventions will be tested by treating the end nodes of the regression tree as categories in a standard subgroup-meta-analysis. This approach will be repeated using both fixed effects and random effects models.

Summary of findings

We will create 'Summary of findings' tables to provide the key information presented in the review for the behavioural change intervention versus any control comparisons, using GRADEpro software (gradepro.org). We will include the following outcomes, which are of most clinical relevance, in each table: i) Habitual PA; ii) Initial claudication distance/time; iii) Maximum claudication distance/time; iv) Mortality; v) Cardiovascular events; vi) Quality of life; and vii) Disease progression outcomes.

We will assess the certainty of the evidence for each outcome as high, moderate, low or very-low based on the five GRADE considerations of risk of bias, inconsistency, indirectness, imprecision, and publication bias, using the GRADE approach [54]. Two researchers will independently judge the certainty of the evidence and, if required, we will resolve any disagreements by consensus or discussion with a third researcher. We will justify all decisions to downgrade the evidence using footnotes and we will make comments to aid the reader's understanding of the review where necessary.

4.35 Feasibility and acceptability review methodology – Systematic review 2

Studies examining the feasibility and acceptability of interventions have a key role in understanding how factors facilitate or hinder the effectiveness of health interventions and how intervention processes are perceived and implemented by users. The focus of this review is to understand the feasibility and acceptability of interventions containing behaviour change techniques for people with IC and intervention providers, but to understand this, we may also examine wider themes relating to patients' experience of living with IC.

Approach: We appreciate there are many approaches to qualitative studies synthesis, with differing philosophical stances underlying each approach [61]. Given that we aim to synthesise data that are relevant to informing policy and practice, we will adopt a pragmatic approach to this qualitative review. Our pragmatic approach is informed by the 'realist' philosophy [62], as we are focused on finding out not only 'what works' in terms of behavioural change interventions for people with IC and intervention providers, but also 'for whom, and under what circumstances'. We will first group feasibility and acceptability data together to provide a tabular summary for narrative synthesis of the included articles, and where possible, quantitative data will be pooled for statistical analysis. For qualitative data, we will employ deductive and inductive analytical approaches throughout the review process, and will also utilise aspects of methods such as critical interpretative synthesis [63]; thematic synthesis [64]; and analytical approaches developed from methods of inquiry such as grounded theory [65].

Initial research questions: Our broad initial research questions for the review of qualitative evidence will include: 1) "What is it like to engage with (or be a provider for) interventions containing behaviour change technique for PA for people with IC?" and 2) "What is it about behaviour change interventions to increase and/or maintain PA in people with IC that make interventions beneficial or not beneficial". Given that the analysis will be conducted iteratively, these questions may be refined and supplementary questions may be added.

Search strategy: See section 4.33

Initial inclusion and exclusion criteria

Study design: We will include:

A. Studies linked to eligible RCTs and non-randomised intervention studies in review 1 and reporting on feasibility and acceptability data including qualitative and mixed-methods studies;

B. Qualitative studies not linked to any specific intervention that draw on the experiences and perceptions of people with IC (and/or providers involved in their care).

All studies must include adults with PAD (and/or the views of providers involved in their care) and must consider issues relating to PA. From our previous systematic reviews in this area[15][14], we know there is a large body of published literature which has explored experiences and perceptions of living with PAD. To gain the most relevant data for this review (whilst also ensuring we generate a manageable amount of qualitative data for analysis within the timescale of the project), we will initially focus on only those studies that explicitly included the views of participants with IC undergoing management which includes a behaviour change element (Category A studies). However, if we find that very few studies in this category have been specific about included participants' IC status and/or interventions with behavioural change elements, we will include studies from the broader literature that have explored patients' experiences and perceptions of PAD, provided they report data specifically relating to views/experiences about PA (Category B studies).

Screening and data extraction and analysis: Two researchers will independently screen identified titles and abstracts and where there is disagreement regarding eligibility, the full paper will be retrieved. Disagreement will be resolved by reaching consensus and further consultation at a research team meeting if required.

Two researchers will independently group the identified studies into the categories A and B described above. Separating intervention studies from non-intervention studies is a feature of the Evidence for Policy and Practice Information and Co-ordinating Centre (EPPI-Centre) mixed synthesis process [66]. Given that the focus of our broader systematic review is to assess the evidence for behaviour change interventions for PA in people with IC, we believe that grouping the studies in this way will facilitate the integration of the quantitative and qualitative review processes. We will then undertake a cyclical, sequential analysis following an approach previously used in an HTA evidence synthesis report [67].

This will entail firstly analysing feasibility and acceptability data from Category A studies by grouping data together to provide a tabular summary for narrative synthesis of the included articles, and where possible, quantitative data will be pooled for statistical analyses.The cconstant comparative method will then be used to identify and understand aspects of the intervention processes and context that relate to our research questions. If indicated, this will be followed by the use of theoretical sampling to identify and analyse Category B (non-intervention studies) studies to confirm or refute the emerging themes and concepts identified during analysis of Category A studies.

For each included study, we will extract data including the aims, methods, populations involved, among others, into a standardised data extraction form. We will then conduct a thematic analysis of the content of the included studies. This analysis will start with a close reading of the study to identify main recurring themes, followed by the generation of higher level themes capturing the phenomena described in the literature and mapping the relationships between them. This process will involve constant comparison of the emerging theoretical structures with the data from the analysed studies. Two researchers will independently undertake the initial reading and coding and will discuss any disagreements until consensus is reached.

Quality assessment

Given that included studies ranged across quantitative, qualitative and mixed method studies, two researchers will independently assess the risk of bias in included studies using the Mixed Methods Appraisal Tool (MMAT), which was designed for the quality appraisal of quantitative, qualitative, and mixed-methods studies included in systematic reviews [Hong 2018]. Disagreements on the results of the quality assessment were resolved by discussion or additional consultation with a third review author.

4.36 Integration of findings of Systematic Reviews 1 and 2

Methods for integrating quantitative and qualitative research evidence in a systematic review is a rapidly developing field, and there is no one consensus approach[66]. Integration of the two reviews will be informed by realist philosophy which acknowledges the complexity of health care interventions and also emphasises the importance of context and mechanisms to explain programme outcomes. Our method will follow the convergent segregated approach according to the JBI methodology for mixed methods systematic reviews [70] to produce a detailed summary of the effectiveness, context (for whom, under what conditions), and how mechanism/theories (how the content and processes) of the interventions affect

increase/maintenance of PA. This will involve quantitative evidence and qualitative evidence being juxtaposed and organised/linked into a line of argument to produce an overall configured analysis. We will present findings narratively where configuration is not possible.

There is an increasing awareness of the importance of a multi-domain approach for understanding PA in IC[15]. An emerging body of literature has highlighted the importance of incorporating broad socioecological and physical contexts in PA interventions for IC to build capability and create opportunities for more sustainable PA change[15][71]. Therefore, we will integrate qualitative and quantitative findings using the social ecological framework and our methodological approach will investigate factors relating to the ***macro***, ***meso*** and ***micro*** level influences and the perspectives and experiences of people with IC related to engaging in and maintaining PA. By ***macro level*** influences we mean the wider social, environmental, cultural, economic and political factors that overarch and influence the ***meso level*** interpersonal influences including interaction with healthcare providers/system, community, family, friends, peers; whilst ***micro level*** influences refer to an individual's health-related factors and decisions about increasing and maintaining habitual PA.

Figure 2 (Below) illustrates how **systematic reviews 1 and 2** will be brought together. Thus, **systematic review 1** with coding of intervention content and meta-regression analyses will provide evidence on the features of effective interventions and their limitations for transfer into UK NHS practice (e.g. what works, for whom, how can this be delivered). **Systematic review 2** will provide evidence on the feasibility and acceptability of interventions.

Timelines: Setting-up & finalising review protocol (prefunding M1-3), studies search & screening (M4-8), data extraction & analysis (M9-20), reporting (M21-27).

Figure 2 - Details of project timelines and integration of project

Aug-Oct 2021 *Months 1>3*	Nov 2021-Mar 2022 *Months 4>8*	Apr 2022 - Mar 2023 *Months 9>20*	Apr-Jun 2023 Months 21-23	Jul-Oct 2023 *Months 24-27*

<table>
<tr>
<td rowspan="2">Set up</td>
<td colspan="2">→Systematic review 1 – About 25 RCTs & non-RCTs data extraction, quality assessment, detailed behaviour change technique coding, data analysis, commence report analysis, commence report</td>
<td rowspan="2">Complete

reviews, meta-analyses

and

↓meta-regression

↗

Mixed-methods

↗synthesis</td>
<td rowspan="2"></td>
</tr>
<tr>
<td></td>
<td>Systematic review 2 – about 13 qualitative and mixed-methods studies, quality assessment, data extraction, data synthesis, commence report</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Prepare final report, conference submissions, papers, info-graphs/ video/podcast</td>
</tr>
</table>

5. Dissemination and outputs

Dissemination is an important aspect of this project and our monthly team meetings will include an ‘Impact Plan’ as a regular agenda item in order to plan a solid dissemination strategy. This will include disseminating the results to researchers (through sharing data and results, with evidence for improving research), to policy makers (evidence that may help improve guidelines for supporting people with IC and for improving research), providers (evidence that may improve patient support) and patients, carers and members of the public (evidence on what patients, carers and providers can do to optimise self-management). We will utilise contemporary methods of dissemination, alongside traditional methods.

Infographics/podcast: We will work in collaboration with the Glasgow Caledonian University visual media team to present the findings in infographics and to produce a short podcast. Our dissemination strategy developed in collaboration with our steering group will identify specific

relevant stakeholders for the infographics/podcast. However, there are five possible audiences that could influence how we present the review findings in an infographic: patients, general public, NHS management representatives/commissioners, expert health professionals, and policy makers. We will tailor the content of the infographics to target each of these five audiences. The team (UA, CS) have undergone training and have worked with the GCU media and visual team in non-traditional dissemination and found this to be a very successful, good value and accessible dissemination strategy. The infographics/podcast will be posted on YouTube as well as links sent to relevant stakeholders. In addition, hard copies of the infographics will be available and distributed to NHS authorities and charities groups.

Conference presentations/workshops: We plan to present results of the project at the annual NICE conference, the annual NHS Scotland conference, UK Vascular Societies' Annual Scientific Meeting and UK Chartered Society of Physiotherapy annual conference. We plan to host workshops at the above conferences, allowing all the results to be presented together.

Open access publications: We will produce a full report to the NIHR (Health Technology Assessment) and plan at least two primary open access publications, one reporting the finding of the quantitative review and meta-analysis and one reporting the integrated synthesis, submitted to open access journals (e.g. European Journal of Vascular and Endovascular Surgery; Implementation Science).

Targeting clinical education and management: We will work with our varied contacts in medical, allied health and nursing to introduce the infographics to a diverse audience for clinical education.

Contemporary technology: We will use contemporary technologies (e.g. Twitter, Youtube) to engage a wide and diverse audience. For example, we will post a summary of the research and link to the infographics/podcast on Twitter, YouTube and relevant websites such as the Circulation Foundation. We will ask contacts to share the link with relevant stakeholders. Our dissemination strategy, developed alongside our steering group, will be used to identify relevant links.

The Conversation: We will write an article for The Conversation about the review findings. The Conversation publishes news and views from the academic and research community directly to the public, given the public a better understanding of complex issues with the hope facilitating a better quality of public discourse and conversations, and to achieving a global

reach. Members of our team (DS, JM, PD) have previously written articles for The Conversation and found this to be a successful strategy in reaching the right target audience, including the general public.

6. PLAN OF INVESTIGATION AND TIMETABLE

For the timetable and milestones please see **Figure 2**.

7. PROJECT MANAGEMENT

The Chief Investigators (UA and DS) are based at the Centre for Living School of Health and Life Sciences, Glasgow Caledonian University, which is where staff employed on the grant will be based. Both chief investigators and three co-applicants (CS, PD, JM) are members of the Active Living Hub of the Ageing Well Research Group. SR is attached to the Clinical Biostastistics Unit, Division of Population Health, Health Services Research & Primary Crare The University of Manchester. CF with over 10 years of experience, works as Information Specialist/System Review Methodologist, Cochrane Vascular Group at both the Usher Institute University of Edinburgh and Cochrane Dementia and Cognitive Improvement Group at University of Oxford Radcliffe Department of Medicine. TG is based at Department of Nursing and Midwifery, University of the Highlands and Islands. The research team have extensive experience undertaking systematic reviews, including quantitative, qualitative data synthesis and integrative review (UA, DS, PD, CS, TG), as well as coding BCTs (UA, DS, JM) and assessing and handling control group variability in bivariate mixed-effects meta-regression models (SR).

The management of the project will be coordinated by the School of Health and Life Science Glasgow Caledonian University team, led by UA and DS. DS has vast experience leading multidisciplinary teams. Frequent, regular communication, including at least monthly teleconferences will be held for all applicants and researchers on the project. All applicants will adhere to standard University procedures, e.g. registration of the systematic review on Prospero database, confidentiality of final report required by NIHR.

7.1 Contributions of research team

Dr Ukachukwu Abaraogu *(PI, 0.15 FTE)* is a qualified Health and Care Professions Council registered physiotherapist with over 12 years of experience across clinical, teaching and research positions. He has clinical and research interest, experience and expertise in long-term conditions. He has extensive experience of conducting systematic reviews, and a track

record of leading both quantitative and qualitative systematic reviews to inform the development of complex interventions (e.g.1–3) He is the principal investigator, will be responsible for the overall project management and reporting, will be responsible for successful completion in line with agreed protocol and will supervise the research assistant. He will also act as the first independent reviewer for screening, data extraction, risk of bias assessment, data analysis and reporting.

Professor Dawn Skelton *(5%FTE)* has vast expertise in developing, delivering and evaluating physical activity interventions in older adults and people with chronic conditions using behaviour change theories and techniques. She is co-PI and will mentor the PI on project management, including the PPI activities, meetings and events. She will also act as a third reviewer to mediate in case of disagreement in article inclusion and data extraction.

Candida Fenton *(0.5hr/wk)* is an Information Specialist and Systematic Review Methodologist at the Universities of Oxford and Edinburgh. She works with the Cochrane Vascular and Cochrane Dementia and Cognitive Impairment Groups, UK, undertaking searching for Systematic Reviews in the clinical and social sciences, across a range of subject areas. She will be a consultant to assist with the development and implementation of the search strategies.

Professor Trish Gorely *(5%FTE)* has a main research interest in psychological and behavioural aspects of physical activity, and has experience in developing physical activity behaviour interventions in people with IC. She will assist in screening eligible studies, data extraction and interpretation related to intervention contextual features, as well as assist in interpreting and reporting review results.

Dr Joanna McParland *(5%FTE)* is a registered Health Psychologist with the Health and Care Professions Council, and an Associate Professor in Psychology at GCU. She is experienced in analysing intervention components and theoretical domains/mechanisms of action. She will assist in coding intervention components/BCTs and theoretical domains/mechanisms of action, will also assist in interpretation of findings and reporting.

Dr Philippa Dall *(5%FTE)* is a senior research fellow with expertise in the measurement of physical activity data. She will work during the last 6 months of the project and will provide advice on the data extraction, analysis and interpretation of physical activity outcomes.

Dr Chris Seenan *(5%FTE)* is a physiotherapist and Senior Lecturer at GCU, with expertise in the qualitative research, design and evaluation of patient educational interventions for patients with IC. He is the CI to the PrEPAID feasibility study from where we recruited our patient PPI members. He will assist with systematic review 2 to screen studies and as second reviewer to extract qualitative data in addition to providing overall advise on interpretation results and dissemination as a member of the Advisory Group.

Dr Sarah Rhodes (replacing Dr Andrew Elders who left GCU and the team) *(5%FTE)* is a experienced Statistician at The University of Manchester Clinical Biostatistics Unit with a wealth of experience and expertise in meta-analysis. She has worked on many meta-analyses of trials about behaviour change intervention in the clinical settings using innovative statistical methods. She will provide advice on statistical design, data synthesis including meta-analysis, interpretation and reporting.

Cathy Gormal *(Costed under PPI)* is a patient living with IC, and is also a retired information specialist. She has contributed in developing the application, and will provide patients perspective in addition to helping with identifying and locating relevant studies, interpretation and reporting.

8. ADVISORY GROUP

The project team will be supported by an Advisory Group with a range of stakeholders including people with IC, NHS authorities, allied health professionals and vascular specialists. We are well networked to a range of organisations, including the largest NHS services in Scotland (covering Edinburgh, Glasgow and Lanarkshire) (DS, AU, CS), and vascular charities, including Circulation Foundation (JB) which will provide a member for our Advisory Group. Two lay members (Cathy Gormal and Jeremy Dearling) who provided input on the application and helped draft the plain English summary have also agreed to participate in the Advisory Group. We have four additional advisors who have agreed to participate in the Advisory Group:

Professor Julie Brittenden is a Professor of Vascular Surgery at the University of Glasgow, Consultant Vascular Surgeon at Queen Elizabeth University Hospital. She is also Director of Research and Development NHS Greater Glasgow & Clyde, and Director of Glasgow Clinical Research Facility. She has provided input into the review questions and protocol. She will be involved throughout the project as a key member of the Advisory Group. She will provide

support/advice throughout the review and will help in the interpretation of the review with a clinical focus on the results, implementation and impact.

Fairer Kimberley is an Advanced Practice Vascular Physiotherapist, and Physiotherapy Team Lead Vascular and Emergency Service John Radcliffe Hospital at Oxford University Hospitals NHS Foundation Trust. She has provided input into the protocol of the review and the application and has also agreed to be part of the Advisory Group.

Jeremy Dearling, lay adviser, is a retired staff nurse with a long term condition and brings the advantage of the perspectives of having been a patient, with the insights into lasting disability, critical illness and the rehabilitation process. He also brings the perspective of having been a front-line NHS employee who understands how wards and hospitals work in real life. He has been involved in PPI since July 2012, has sat on several research panels including the British Heart Foundation, and the Stroke Association, has reviewed for the Eastern Academic Health Science Network, the Research Design Service, and the NIHR. He will provide valuable assistance in the PPI including mentoring other patient PPI members.

On successful grant award, we plan to include at least two commissioners of IC services as part of our Advisory Group. Additional group members may be sought from the vascular health and person-centred management hub affiliated with the Ageing Well Research Group at Glasgow Caledonian University (led by CS) and other organisations where JB (e.g. NHS Greater Glasgow and Clyde, Research Council of the Vascular Society of Great Britain & Ireland, NHS research priorities to HTA interventional procedures panel) and DS (e.g. Public Health England, NHS Lanarkshire) are involved in priority setting activities.

The purpose of the Advisory Group is to ensure the importance and relevance of the findings for those who are living with IC, people who support them, NHS services, and health professionals who manage people with IC. The group will also help to disseminate the findings widely amongst their networks. Due to the COVID-19 situation, we plan virtual meetings for the grant applicants, research team and Advisory Group at the beginning of the project, where we will describe the project and seek input into the protocol. During the project there will be 4 virtual meetings to discuss the research evidence as it emerges, to discuss further research that should be undertaken by us for the project, and the interpretation of the results. At the end of the project there will be further virtual meeting, where a draft of the final report will be discussed. All members of the Advisory Group will be invited to have authorship on the report. In particular, the Advisory Group will help ensure that the review is conducted in a systematic

and transparent manner; check for over-interpretation of data; provide opinion on the credibility and plausibility of the thematic index and other emergent issues; and have the opportunity to provide sources of disconfirming data.

9. ETHICAL ARRANGEMENTS

Ethical approval is not required for this project.

References

Hong, Q.N., Fàbregues, S., Bartlett, G. et al. (10 more authors) (2018) *The Mixed Methods Appraisal Tool (MMAT) version 2018 for information professionals and researchers.* Education for Information, 34 (4). pp. 285-291. ISSN 0167-8329

Figure 1: Initial system-based logic model of behavioural change intervention for physical activity in intermittent claudication