A randomised controlled trial and economic evaluation of a community-based physical activity intervention to prevent mobility-related disability for retired older people. The REACT (REtirement in ACTion) study

Research Protocol

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Chief Investigator: Dr Afroditi Stathi, University of Bath

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1. Title: A randomised controlled trial and economic evaluation of a community-based physical activity intervention to prevent mobility-related disability for retired older people. The REACT (REtirement in ACTion) study

2. Background: ***2.1. Existing research:*** A significant challenge for public health in England is to develop effective strategies to promote health and well-being in the expanding older population. More than 720,000 people turned 65 in 2012, and the percentage of people aged 65 and over is the highest in UK history[1,2]. During old age, there is a population-wide transition from independence and adequate physical function towards frailty, mobility-related disability and an increased demand for health and support services. Mobility-related disability results in an increased need for support, such as meal delivery, help with housework and the need for residential care, and an increased risk of falls due to a loss of leg muscle strength and balance. The prevalence of mobility-related disability increases rapidly with age and is a major source of health and social care costs[3,4]. Interventions that can reduce or reverse this functional decline will therefore improve quality of life, mental well-being in older people and reduce demand on health and social services[5]. Physical inactivity is one of the strongest predictors of mobility-related disability in older adults[6,7]. Prospective cohort studies demonstrate that a higher level of physical activity is associated with a lower risk of physical disability[8-13]. A fit and active older person has 36% lower risk of developing functional limitations and 38% lower risk of hip fracture[14]. Of the 6,200 older persons who were disability-free at baseline in the longitudinal EPESE cohort study, those in the lowest tertile of regular physical activity were 1.8 times more likely to develop problems with Activities of Daily Living (ADLs) or mobility-related disability over 4 years than those in the upper tertile[15]. In the UK-based OPAL plus cohort study, older people who undertook at least 25 minutes of moderate or vigorous exercise every day at baseline needed fewer prescriptions and were less likely to be admitted to hospital in an emergency four to five years later[16].

Unfortunately, older adults are the least active segment of the UK population. Less than 30% of 65-74 year-olds report any moderate intensity physical activity lasting at least ten minutes in the previous four weeks [17]. Health Survey for England data indicate that people whose lower-limb physical function is declining, but who otherwise remain reasonably healthy make up a large proportion of older adults - 14% of men and 25% of women aged 65 were classified as 'walking impaired' (defined as having a walking speed of less than 0.5 metres per second) [5,18]. This rose to 36% of men and 56% of women by age 85. The ability to balance well also declined strongly with age for both men and women. Among people aged 65, 36% of women and 27% of men reported a need for help in the last month with one or more ADLs such as getting up and down stairs, dressing, getting around indoors, or shopping for food. These people are in transition from independence to frailty and have a great deal to gain if loss of function can be reversed and independence maintained [17]. Indeed, the beneficial effects of physical activity and strength-and-balance training programmes on functional outcomes in older adults have been conclusively demonstrated[20-23]. For instance, in the FAST RCT [21] an 18-month aerobic exercise or resistance exercise training programme significantly improved physical function and ADLs in community dwelling older adults with knee osteoarthritis[24]. Physical activity programmes have also improved physical function and objectively measured mobility (distance walked in 6 mins) in patients with chronic obstructive pulmonary disease [25] or heart failure [26-27]. A structured strength exercise programme among frail older persons significantly improved functional mobility, gait speed and muscle strength [28,29]. Particularly pertinent to this proposal is the LIFE study, a single-blind, multicentre randomised controlled trial of a community-based physical activity intervention in 1635 sedentary adults aged 70-89 conducted in the USA[30]. This intervention reduced the incidence of major mobility disability (defined as the inability to complete a 400-m walk test within 15 minutes without sitting or help from another person)[30] (Hazard Ratio [HR] 0.82: 95%CI, 0.69-0.98) and persistent mobility disability (major mobility disability at consecutive timepoints) (HR 0.72: 95%CI, 0.57-0.91) at a mean 2.6 years of follow up. The intervention group maintained a 40-min/wk difference (95% CI, 29 to 52; $p < .001$) in moderate intensity physical activity assessed with accelerometry, compared with the control group at 24 months of follow-up. There was no significant difference in adverse events. These estimates are likely to be conservative as the control group received a substantial health education/lifestyle intervention including weekly workshops for 6 months and monthly sessions thereafter.

*Gaps in the evidence***:** There is convincing evidence from prospective cohort studies and high quality RCTs that increased physical activity can prevent or reverse decline in physical function and reduce mobility-related disability. An intervention developed in the US has shown promising results in promoting long-term increases in physical activity and reducing mobility-related disability. However, there is a need for evidence about the effectiveness and cost-effectiveness of similar programmes tailored for a UK population of older adults who are at risk of losing functional mobility.

2.2. Risks and benefits: The benefits of moderate intensity physical activity for older people vastly outweigh the risks[31]. The UK Chief Medical Officer's [CMO] guidelines for physical activity for older adults concluded that "engaging in physical activity carries very low health and safety risks for most older adults. In contrast, the risks of poor health as a result of inactivity are very high"[32 (pp 32,38)]. Risks occur predominantly among those undertaking vigorous activity or contact sports. In rare cases, inactive and unfit individuals who start doing vigorous physical activity may face increased cardiovascular risks and there are some important counter indications such as unstable cardiovascular illness or uncontrolled hypertension.

The proposed REACT exercise protocol will emphasise principles of progression to achieve steady improvements in strength and aerobic capacity. Following CMO guidelines, moderate intensity activity will be tailored to current capacity and vigorous intensity activity levels will be avoided. Participants will also be taught how to use ratings of perceived exertion to judge the relative intensity of their activity[33-35]. All sessions will be led by professionals trained to deliver exercise for older adults in a safe manner. Both the CMO's guidance[32] and NICE guidelines[36] emphasise that increasing engagement with physical activity would provide considerable benefit in terms of both human welfare and savings in social and health care costs. As well as preventing mobility-related disability, the evidence is strong that physical activity protects against cardiovascular disease, diabetes, and some cancers[37]. Prospective cohort studies indicate that activity in later years also delays cognitive decline, and reduces the risk of depression, dementia and Alzheimer's disease[38,39]. Intervention studies indicate that in older adults, exercise also improves cognitive abilities[40], reduces risk of falls in those at risk[41], and alleviates depression[42].

2.3. Rationale for current study**:** Breaking the spiral of decline that is characterised by loss of physical and cognitive function, reduced capacity to independently manage daily tasks, and reductions in social interaction is fundamental to healthy ageing. It also has the potential to substantially reduce reliance on health and social care services. This is particularly true for those who are at risk of mobility-related disability resulting from low levels of physical activity as they settle into changed routines after their primary working years. There is clear evidence that physical activity programmes are capable of reducing or even reversing this decline. There are existing activity promotion schemes (e.g. Fit for the Future) and programmes for falls prevention, treatment of dementia or depression within specific settings such as residential care. However, there have been few attempts to develop and rigorously evaluate feasible models of physical activity promotion for older people in community settings. In particular, there are no programmes that specifically target people at high risk of mobility-related disability, and few programmes are grounded in service user and service provider perspectives[3]. REACT will target the non-disabled but high-risk segment of the older population with an intervention to reduce mobility-related disability. This approach has many advantages. As shown in the LIFE Project, people in this category are still physically capable of engaging in a progressive exercise programme and have potential for prevention of further physical decline. A programme that can successfully engage them in sufficient activity to improve strength, aerobic capacity, coordination and balance would have a major impact on their prospects for sustained health and independence. The eligibility criteria in this study are therefore aimed at identifying persons with current low levels of activity, who have high risk of mobility-related disability (as assessed by a battery of objective physical performance tests), but who have not yet developed disability.

Development of a "best-bet" intervention: This proposal builds on several years of multidisciplinary work by this team aimed at understanding influences on the adoption and maintenance of physical activity in community-based activity programmes. This included 'Better Ageing', a multicentre

intervention study funded by the European Union Framework V programme[43,44]. This study provided indications of strategies for successful recruitment and retention with a 91% adherence rate achieved at 12 months. However, very few people continued being active after programme completion, emphasising a need to encourage transition from centre-based activities to independent and lifestyle-based physical activity that is sustainable in participants' day to day lives[45,89]. The OPAL cohort study (and OPAL-PLUS follow-up) examined patterns of objectively measured physical activity and influences on physical activity in a UK sample of people aged over-70[47]. This provided data on levels and rates of decline in mobility-related disability and physical activity as well data on social, psychological and environmental barriers and facilitators of physical activity in older people. Following these studies, our recent cross-Research Council funded Avon Network for the Promotion of Active Ageing in the Community (AVONet) used literature reviews, focus groups and workshops with service providers, older people, international experts and service commissioners to assess the needs of older people and their communities for physical activity promotion[48]. The AVONet produced a widely disseminated guidance for local decision-makers on the promotion of physical activity in older people[48]. The AVONet guide identified a) key social, psychological, behavioural, and environmental barriers to the adoption and maintenance of physical activity in older people b) appropriate theory and evidence for interventions and c) three 'best bet' solutions for effective promotion of active ageing in UK communities. A structured, community and group-based activity programme featuring a strong social programme emerged as the favoured candidate. The LIFE project in USA, the largest trial of its kind with a sample of 1635 older people has provided a) 'proof of concept' evidence (i.e. that increasing physical activity in older people strongly reduces functional disability), and b) evidence of successful recruitment and retention of older people (at least in US community settings)[30]. The intervention content addresses the barriers to adoption and maintenance identified by AVONet, and it was considered by our service user, service provider and commissioner stakeholders to be suitable for delivery across a range of socio-economic and cultural populations[48]. The LIFE intervention therefore provides us with an ideal starting point for an intervention to promote physical activity to prevent mobility-related disability in older people in UK community settings.

In summary, one of the most important determinants of quality of life and of health and social care costs in our aging population is mobility-related disability [49], which in turn is strongly affected by physical activity. People who maintain a basic level of muscle strength and aerobic capacity are able to engage with ADLs and to continue living independently. This has considerable implications in terms of quality of life and social and health care costs. Previous research has a) developed an intervention to reduce mobility-related disability through physical activity (the LIFE intervention) and b) established 'proof of concept' by demonstrating its effectiveness to reduce mobility-related disability. The proposed study now aims to adapt the LIFE intervention for use in a UK setting, and conduct a full-scale pragmatic multi-centre randomised controlled trial with 24-month follow up to assess its effectiveness for reducing mobility-related disability and its cost-effectiveness for use in the UK.

3. Research Objectives: The primary aim of the REACT study is to assess the effectiveness and cost-effectiveness of a community-based physical activity intervention for reducing the progression of mobility-related functional limitations in older people who are at high risk of transition from independence to mobility-related disability.

Objectives:

1. To adapt the LIFE intervention from the USA, for use in UK community settings. This work will be completed in parallel with project set-up procedures (Months 1 to 5).

2. To conduct an internal pilot study to evaluate and optimise the feasibility and acceptability of the REACT intervention to older people and intervention providers and of the proposed trial methods across a diverse sample, spanning multiple ethnic groups and areas varying in deprivation index. (Months 5 to 12 (and then data becomes part of the main trial)).

3. To conduct a full-scale pragmatic multi-centre randomised controlled trial of the REACT intervention with data collection at 0, 6, 12 and 24 months of follow up (Months 13 to 52).

4. To conduct an economic analysis including estimates of the resource use and costs associated with delivery, and cost-effectiveness of the intervention.

5. To explore how intervention effectiveness varies with deprivation index and ethnicity (i.e. to explore potential effects on health inequalities).

4. Research Design: The REACT study is a multi-centre pragmatic two-arm parallel-group randomised controlled trial with an internal pilot phase[50] comparing the REACT intervention with a minimal intervention control condition, and having a follow-up of 24 months.

Primary hypothesis: Compared with the control group, participants allocated to receive the REACT programme will have significantly reduced mobility-related limitations, as indicated by SPPB score, at 24 months of follow-up.

Secondary hypotheses: Compared with the control group, participants allocated to the REACT programme will significantly increase their levels of moderate intensity physical activity, health-related quality of life, cognitive function, physical functional ability, mental well-being and have reduced fatigue at 24 months.

4.1. Randomisation: Eligible participants will be randomised to one of the two arms via a centralised web-based randomisation service provided through the Peninsula Clinical Trials Research Unit (see attached Flow Chart). The randomisation sequence will be generated by the online programme and will use a minimisation algorithm to balance groups in terms of age group, gender and initial functional ability.

4.2. Previous pilot studies: In the LIFE-P pilot study, 424 sedentary older people aged 70-89 were randomised to a physical activity intervention or a standardised health education intervention [19]. The 12-month follow-up data provided evidence that the LIFE intervention a) increased physical activity (moderate intensity activity increased by 291 kcal ($p<0.002$), which is equivalent to 88 mins /week of brisk walking) and b) compared with controls, significantly increased mobility-related functional ability measured by the Short Physical Performance Battery (SPPB) and 400m walk speed. A longer-term follow-up study on a sub-sample of 106 participants showed that changes in moderate intensity physical activity were maintained 24 months after the end of intervention (66 mins /wk more than controls, $p<0.05$). The subsequent LIFE main trial established the effectiveness of the intervention in reducing both major mobility-related disability and persistent mobility-related disability (see definitions in Section 2.1). These prior studies will inform the recruitment, measurement and intervention procedures for REACT. These two studies also established the feasibility of recruitment, intervention delivery and retention procedures in US settings, as well as the intervention safety profile and the validity of methods for defining mobility-related disability. However, we need to establish the feasibility of recruitment and intervention delivery, as well as effectiveness and cost-effectiveness in UK community settings.

4.3. Stopping rules or discontinuation criteria: The Trial Steering Committee, with advice from the Data Monitoring Committee, will assess the feasibility of the trial at 12 months of follow-up during the internal pilot phase, taking into account findings on the acceptability of trial procedures, intervention adherence and recruitment and retention rates. Based on our recruitment rates in previous UK-based physical activity interventions with similar target populations (Project ACE, Better Ageing) and with two part-time (0.5 FTE x 2) research assistants at each of three sites, in the pilot study we anticipate a recruitment rate of 15 participants/month/site, (180 participants will be recruited in total over 4 months). If the recruitment rate is less than predicted in a given month, we will take actions to increase it (increasing the number of people approached and/or increasing the geographical area, adapting recruitment procedures). Retention rates (proportion of people providing follow up data) will be checked at 6 months and 12 months for the pilot data. If the recruitment is less than 75% of target by the end of the third month or if retention rates fall below 75% at either 6 or 12 months, we will consider stopping the trial. A further stopping criterion will be receipt of strong negative feedback from the majority of either participants or intervention providers about the intervention or trial methods.

Changes in the recruitment strategy and introduction of new recruitment avenues will be discussed and agreed by the Project Management Group. The participants recruited in the pilot study will be included in the trial analysis.

4.4. Methods to address sources of bias: *i) Allocation concealment:* We will ensure allocation concealment until the point of randomisation which will be after collection of all baseline measures; *ii) Blinding:* It is not possible to blind study participants to treatment allocation in behavioural intervention studies and this is not a problem in pragmatic trial designs, which aim to estimate the benefits of the intervention over and above usual or standardised care[50]. However, we will take steps to ensure that data collectors, statisticians and the participants' healthcare team remain blinded to group allocation. At data collection visits, patients will be asked not to reveal which group they are in. Where possible, at follow-up, the primary outcome (SPPB) will be assessed by a researcher who was not involved in randomisation of the participant at baseline (each site will have multiple data-collecting research assistants, so this can be achieved where logistics allow). Allocation codes will be locked away by the CI until the database is closed for analysis; *iii) Incomplete outcome data:* Measures to maximise retention of participants are described in Section 8. To examine the potential extent of bias due to dropout from the study, intention-to-treat and sensitivity analyses will be conducted using a range of assumptions to impute missing data; *iv) Selective reporting:* We will report analyses for all outcome measures in accordance with a pre-defined analysis plan, which will be submitted to the TSC and published on the ISRCTN clinical trials register prior to data analysis. Any proposed amendments will require approval from the TSC; and *v) Other sources of bias (e.g. intervention bias):* Contamination between patients in different trial arms is unlikely due to the intensive nature of the intervention (i.e. transferability is limited).

5. Study Population: The aim is to target a population with functional limitations who are at risk of major mobility-related limitations, but who are still ambulatory. The study will be conducted at three centres in Bath/Bristol, Devon, and Birmingham, allowing recruitment of a diverse sample including ethnic minorities, and participants from urban, rural and semi-rural locations.

Inclusion criteria: Retired men and women aged 65 or older with a sedentary lifestyle (operationally defined as less than 125 minutes per week of moderate-intensity physical activity based on the modified 18-item Community Health Activities Model Program for Seniors (CHAMPS) questionnaire[53], who are planning to reside in the target area (Bath/Bristol, Devon, Birmingham) for at least 24 months. Participants must also score 8 or less on the Short Physical Performance Battery (SPPB)[54]. This is based on data showing that older adults with SPPB scores of 8 or less have substantially higher risk of major mobility disability three years later (OR = 7.7 (95%CI: 2.3 to 26.0) compared with those who score 12 [30,53]. Our data from the OPAL study show that 27% (64/240) of recruited UK adults over 70 scored 8 or less on the SPPB and data from HSE show that more than 80% of adults aged over 65 report fewer than 150 mins/wk of moderate physical activity[55]. Hence, we have estimated that around 20% of adults aged over 65 will meet both these criteria. During the pilot phase we will monitor the baseline profiles of participants and consider whether the inclusion /exclusion criterion need refinement (e.g. if they lead to over-exclusion of participants).

Exclusion criteria: People will be excluded if: a) they have a diagnosis of dementia or score less than 80 on the Modified Mini-Mental State Exam (3MSE) indicating inability to give informed consent; b) participation in moderate activity is deemed to be unsafe based on assessment with the EASY tool[56]; c) a documented or patient-reported medical condition that would preclude participation, including (but not limited to) severe uncontrolled arthritis, awaiting knee or hip surgery, lung disease requiring use of corticosteroids or supplemental oxygen, unstable cardiovascular disease including unstable angina, uncontrolled and symptomatic cardiac arrhythmias, past history of cardiac, neuromuscular/musculoskeletal/ rheumatoid disorders that are exacerbated by exercise, or severe uncontrolled psychiatric illness; d) self-reported inability to walk across a room; e) existing major mobility limitation. This will be defined using a SPPB lower cut-off score (e.g. 3 or less). The exact cut-off will be decided based on evidence of ability to benefit from the intervention for people with different SPPB scores from the LIFE trial. In addition, being unable to complete the 4m walk component of SPPB will result in exclusion (this is an objective check on the self-report criterion used

at telephone screening (item d above); f) current involvement in other research or regular (at least weekly) exercise programmes that aim to build lower limb capacity or fitness (e.g. walking programmes).

In summary, we will recruit inactive, community living, older persons aged 65 and over, who are at risk of major mobility-related limitations but who are still ambulatory. This characterises around 20% of the over-65 population in the UK (of whom we expect around 30% will be excluded using the above criteria)[30].

6. Socioeconomic deprivation and inequalities: Sedentary behaviour and mobility limitations in older people are more prevalent in socio-economically deprived sectors of the population[57]. Ethnic minorities experience significantly greater risk of a range of physical and mental health problems as compared to their white counterparts, and subsequently suffer higher rates of morbidity and premature mortality[58,59]. Self-reported data from the HSE indicate that older (55+yrs) Bangladeshi, Pakistani, and Indian adults are less likely to meet physical activity guidelines compared to their Caucasian counterparts[60]. Thus, interventions that increase physical activity in sedentary and ethnically diverse populations will help reduce health inequalities. The geographical areas in South West England and Birmingham targeted in REACT were chosen to recruit sedentary older people from diverse socioeconomic and ethnic backgrounds, as well as including both rural and urban areas. Our team has successfully recruited people with diverse SES status to a number of previous projects[61-63]. Within each study location, we will target areas for recruitment that include a broad range of deprivation. We will monitor the Index of Multiple Deprivation (IMD) scores of postcodes of the recruited sample quarterly as the study progresses and will seek to over-sample in higher deprivation areas if interim analyses of baseline characteristics at 6 and 12 months in the pilot study show that the recruited sample is not broadly representative of the UK population.

7. Planned interventions

7.1. Intervention Arm: The intervention group will receive a standardised 12-month programme designed for delivery in leisure/community centres and fitness/health clubs where low-cost late morning capacity is available (which coincides with the periods where older adults are most likely to be out and about)[64] and where suitable space for social activities is available. REACT will be delivered by qualified exercise professionals with experience in delivery of exercise classes in the community. We will collaborate with existing community based organisations who have access to appropriate venues and delivery staff. These organisations will offer a range of facilities suitable for delivery of the intervention. Sessions will be organised as group activities with up to 15 participants per group, but there will be individually tailored elements for both aerobic exercise (where intensity will be tailored to existing aerobic capacity /fitness) and strength work (where exercises will be tailored to existing muscle strength). Activities will include cardiovascular, strength, balance and flexibility exercises and daily lifestyle-based activity in the form of neighbourhood walking and active travel. Breaks in sedentary time will also be promoted. Social activities such as post-exercise coffee meetings and community-based activities will be organised to encourage a 'social club' atmosphere.

Using intervention mapping, a rigorous framework for the development of behaviour change interventions[65], we have built on the "needs assessment" work conducted by AVONet[48] to adapt the LIFE intervention to be responsive to the needs and preferences of the target population. Key identified facilitating factors were the need of people to feel more competent and confident, in charge of their own progress, and to socialise and feel part of a fun and friendly environment[48]. The REACT intervention is therefore designed to develop physical confidence, build skills for long term behaviour change, including a focus on neighbourhood activity, and providing opportunities for enjoyable social engagement. A novel element is the accompanying 'REACT ambassadors' scheme that provides the opportunity for participants to develop expertise and contribute as a) a programme recruiter, or b) a local neighbourhood coordinator. Our aim is to produce a pragmatic model of delivery that is rooted in the needs of the local community, that attracts a diverse population of older adults largely through its social and developmental appeal, is increasingly self-sustaining, and that has potential for application across the UK.

Physical activity specification: The programme will be designed to address each element of health-related fitness recommended in the UK CMO guidelines for activity for older adults[32]. This includes warming up, strengthening and flexibility exercises, aerobic exercise building to moderate intensity levels, and exercises designed to improve balance and coordination. The intervention includes a long-term target of 150 minutes of moderate intensity activity per week, which is approached progressively and takes place in part beyond the structured sessions. Participants will be encouraged to seek opportunities for physical activity throughout the day, through active hobbies such as gardening, and use of stairs, leisurely walks with friends and active travel. Supplementary instructions, 'home-friendly' exercises and written materials will be supplied to encourage generalisation of exercise performance to the home environment [67,68]. Principles of progression and adaptation will be applied in order to build exercise training demand at a rate that is appropriate for current levels of function and activity. Participants will be trained to use ratings of perceived exertion and self-assessment of breathing as a method of regulating physical activity to moderate intensity levels[69,70]. The initial focus is to orient participants to the concept of strength training, to build confidence in performing and completing the exercises, and to introduce the concept of training progression. The supervised setting will allow instructors to tailor the programme to individual needs and abilities early on, so as to prevent early dropout and through in-session interactions and discussion to facilitate the building of self-efficacy and support, which have been found to be key to long-term physical activity maintenance[71]. If participants miss two consecutive sessions, REACT leaders will call the participant to problem solve ways for the participant to re-engage with the programme.

Delivery: REACT will be delivered in two progressive phases (Adoption and Maintenance) and established behaviour change techniques will be used to enhance motivation, to make realistic plans for sustainable activity, to pre-empt and overcome barriers, to engage social support and to use self-monitoring and self-regulatory techniques to support the maintenance of behaviour change. REACT will be delivered by qualified exercise professionals with experience in delivery of exercise classes in the community. The REACT co-applicants will provide training in intervention delivery methods, including detailed session plans to ensure consistency and fidelity in programme delivery.

Adoption (weeks 1–8): The purpose of this phase is to stimulate initial increases in physical activity and fitness, to reduce any anxieties or concerns about exercise, and to build confidence and a sense of attachment to the programme. Each participant will receive a 45-minute individualised, face-to-face introductory session, during which time the programme will be described, benefits and personal relevance of activity discussed, questions answered, and baseline assessment used to tailor the programme for starting levels and progression. Two 60 minute physical activity sessions per week, which will include some social time, will then be delivered by the REACT trainer.

Adoption (weeks 9–24): A 45-minute interactive educational/social session run by the REACT trainers will be added at the end of one of the two weekly sessions. These sessions will use evidence-based, person-centred behaviour change strategies to build intrinsic motivation and self-efficacy. They will be designed to maximise enjoyment, social interaction, and group identity [70,72]. Behavioural management will focus on self-regulation using goal setting, self-monitoring, reviewing of goals and problem-solving [71,74]. A key focus will be on exploring and planning transition to more lifestyle-based activities. Pedometers will be introduced during these sessions to support the participant in the transition to the maintenance phase. After week 12, the exercise session frequency will be reduced to one per week but with an expectation that participants find an hour per week to exercise at home or in the neighbourhood. Performance of this transitional behaviour will be encouraged and monitored in the interactive sessions. Bi-monthly newsletters will be disseminated to provide on-going support, educational materials and an opportunity for information exchange. Participants will also be introduced to the REACT Ambassador training programme which will be delivered during the Maintenance stage.

Maintenance: (weeks 25 to 52): The second stage will focus further on home and neighbourhood-based activities. Continued access will be available to one weekly centre-based physical activity session. Participants will enact action plans that were made during the transition phase and will be supported through group meetings once a month. At this stage we will merge multiple groups in the

same area to form larger groups. We will encourage groups to self-organise their own social interaction beyond the scope of the study and to consider doing activities together as part of their ongoing physical activity regime. Participants will be informed about local opportunities for physical activity in the community via our partners at each site and will be offered vouchers for tester activity sessions (supplied by our collaborators and partners, other local service providers /companies, including walk-and-talk groups, bowling clubs, dance classes, and Tai Chi).

This will introduce people to a range of both free and pay-for activities that are available in the local community. All intervention group participants will be offered the opportunity to be trained as "REACT Ambassadors" to help support the long term sustainability of the programme. REACT Ambassadors will have a choice of specialising in programme administration, or becoming local community activators (facilitators of local physical activity opportunities). This will help to facilitate maintenance activities and increase the frequency of meetings in the maintenance stage without adding to intervention costs.

Post intervention: REACT Ambassadors will help to sustain activities after the initial 12 months by organising group meetings and activities. Further 'taster session' vouchers for community based activities will also be provided, and participants will be offered the weekly REACT sessions at a subsidised rate (subject to agreement with providers).This menu of strategies is designed to build and establish a 'brand' that has wide appeal, attract media attention and become increasingly known through recommendation and word-of-mouth, which is the most successful mechanism of recruitment to community-based health promotion programmes[83]. The ambassador programme will promote growth and increasing sustainability. The pilot study will help to embed the intervention in the local community and (through word-of-mouth) facilitate recruitment for the main trial.

REACT aims to be scaled up nationally and implemented in a range of settings ensuring its successful translation to community programmes. During this study, REACT will be delivered in a wide range of community settings to which we have access via our extensive network of collaborators and partners. These may include sports centres but both the space and the equipment requirements for delivering REACT make the delivery of the intervention feasible in any community facility including church halls and other community centres. These may be more appealing to older people than sports centres which usually promote a young, elite sport and performance focused image more appealing to younger populations.

7.2. Control Arm: After completion of baseline assessments, participants allocated to the control group will be given a booklet with social events and activities in their local community and a booklet with health education material focusing on healthy eating. After the completion of the six month assessment, control participants will be invited to one 60-minute group session where they will receive information on a variety of healthy ageing topics including prevention and health care. After 12-month data collection, controls will be invited to a further 60-minute group session and information about local social activity opportunities will be provided. After 24-month data collection, controls will be invited to a final 45 min group session. They will be provided with more information about health and well-being focussing on active living and importance of functional ability, and taster session vouchers for activities in their local community.

8. Methods for recruitment and retention: We will use two main recruitment strategies: A) We will select recipients by age and post-code (and for absence of any searchable exclusion criteria) from GP databases. We will mail personalised invitations, targeting our mailshot to maximise diversity in terms of age and postcode. This was the most efficient recruitment method in both the LIFE study[30,76] and the ACE project [73]. B) To enhance recruitment of ethnically diverse participants in the Birmingham and Bristol areas, we will use word-of-mouth and snowball sampling techniques with the assistance of bi-lingual community champions (via existing community contacts). This strategy has been used successfully by members of the research team and is more successful for recruiting ethnic minorities than recruiting via healthcare professionals[77]. Volunteers from this route will be sent personalised invitations. The eligibility of respondents will be assessed in a three-step sequential process:-

1. Initial self-selection: Study invitation letters will make it clear that we wish to recruit people who have some difficulty walking more than 400 metres (quarter of a mile) without help from another person; or climbing two or more flights of stairs; or moving from sitting in a chair to standing, but who are still able to do these things. The first two criteria have been shown to strongly predict SPPB scores[78] and the third is a self-report of one of the components of the SPPB test battery which correlates strongly with SPPB total score. The performance characteristics of this initial self-screening method are unknown, but the pilot study will allow us to test our assumptions (below) about the proportion of eligible participants following the use of this tool and to refine our approach if needed.

2. Phone based screening: Full study information will be posted to people returning the reply slip, and a preliminary phone screen will assess safety to exercise using the EASY screening tool[56]. We will also check inclusion and exclusion criteria that can be assessed by phone (e.g. self-reported inability to walk across a room).

3. Face to face recruitment sessions: Potentially eligible participants will then be invited to a group-based recruitment session. This method involves having several 'stations' for each step in the recruitment process which participants work their way through and has been successfully piloted in prior studies[73,79]. Attendees will have an opportunity to ask questions about the study and be asked to give written informed consent (including consent for a longer term follow-up at up to 10 years). They will then be administered the SPPB in a private room. Those scoring between a lower cut-off (to be agreed by the Project Management Group) and 8 will be invited to complete the CHAMPS physical activity questionnaire, and the Modified Mini-Mental State (3MSE) questionnaires to further assess study eligibility. Participants who meet the eligibility criteria will be invited to complete the remainder of the baseline assessments. They will be given a questionnaire pack and asked to wear a wrist-worn accelerometer for the next seven days (and return it by post). Following the return of the accelerometer, they will be randomly assigned in a 1:1 ratio to either the intervention or the control group. Interpreters will be available to assist with recruitment and data collection as needed.

Based on community demographic data, we will seek to recruit purposively within each locality to increase recruitment activity in low income and more ethnically diverse postcodes. The recruitment approaches will be supported by a low cost public relations campaign targeting local newspapers, magazines, radio and community events. We will work closely with our collaborators, local community groups, charities and the public sector, using their existing networks to leverage our recruitment process (see letters of support). Publicity materials will be made available through libraries, supermarkets, post offices and GP surgeries, where our AVONet research suggested they were likely to be seen by older adults. We will also use 'word-of-mouth' by encouraging potential participants to pass information to others who may be eligible.

At the start of the study, we will hold a half-day event where collaborators and partners from all sites will further discuss the sampling framework representativeness, share up-to-date information about effective ways for reaching target groups, and identify further partners and community groups which focus on the study population of REACT and will be invited to become partners of the study. All these actions will be further evaluated during the internal pilot stage and any necessary changes on recruitment and sampling framework will be discussed, identified and agreed by the Project Management Group and Trial Steering Committee prior to the start of the main phase of the study.

To achieve the desired levels of recruitment (768) we estimate that we would need to write to around 9000 people over the 14 month recruitment period (see timetable). Of these, based on prior studies recruiting similar populations (Waste the Waist, OPAL) we expect that 22% would respond to the letter and be willing to take part. We would then need to phone-screen 1980 people (47 per site per month). This would exclude a further 20%, leaving us to conduct face-to-face screening procedures with 1580 (38 people per site per month, which would require 3 recruitment group sessions per site per month). We estimate that 40% of these would be eligible (assuming the self-screen questionnaire reduces the proportion of those who are ineligible from 80 to 60%) resulting in a total recruited of 768. Based on preliminary database searches and feasibility discussion with general practices in Bath and Devon facilitated by the Clinical Research Network, the recruitment plan will require recruitment of 5-8

GP practices per site. Recruitment and response rates and sample characteristics will be monitored on a monthly basis. Recruitment procedures will be refined based on this feedback during the course of the pilot study to correct any deviations from sampling targets and target response rates.

Loss to follow up is modelled on an annual attrition rate of 12.5%. This is based on attrition rates in the Better Ageing study and LIFE (6.5% per year) which were both community physical activity intervention studies. The internal pilot study will demonstrate that recruitment and retention rates are satisfactory and established at each site before we progress to the full-scale trial. To maximise retention, we will offer a voucher-based incentive for trial completion (one of the most effective strategies identified by a recent Cochrane Review[66]) and we will follow recommendations for good practice for retention in trials provided by the NIHR School for Primary Care Research[80]. These include emphasising the meaningfulness of the research, regular contact, use of incentives and involving service users in development of study materials.

9. Outcome Measures: The primary outcome will be the Short Physical Performance Battery (SPPB) score at 24 months. SPPB is an objective battery of functional performance tests (observed ability to complete a repeated sit-to-stand task, a standing balance test and a gait speed assessment). The resulting score ranges from 0 to 12. The SPPB can usually be completed in 5 minutes with the use of a stopwatch, a 4-m tape and a chair. Inter-rater reliability is reported as 0.9 and test–retest reliability is 0.72[81]. The SPPB has been shown to predict both mobility-related disability (inability to complete a 400m walk in 15 minutes) and ADL disability (using Barthel Index ADL scores[55,84]). SPPB score provides a reliable estimate of future risk of hospitalisation and decline in health and function in older adults[54,84,85]. Risk of mobility-related disability over a three-year period shows a strong graded response across the range of SPPB scores (OR = 26.9; 7.7; 8.3; 3.4 for SPPB <= 7; SPPB <=8, and SPPB <= 9; SPPB ,=10, respectively[52]. Based on these associations and other data, a 0.5 difference (effect size 0.25) is considered to be a clinically meaningful change in SPPB score[86].

Secondary outcomes: 1. Change in minutes of moderate intensity physical activity, as measured by accelerometer data using a protocol successfully used in previous studies [64]. We will use wrist-worn accelerometers as they provide high compliance rates, minimal burden to participants, and they are waterproof minimising the risk for participants to forget to put them back on after swimming or having a shower (common problems with waist worn accelerometers). Further secondary outcomes are: 2. Sedentary time and breaks in sedentary time per day assessed by accelerometry. 3. Self-reported physical activity (CHAMPS questionnaire) [53]. 4. Hand grip strength of the dominant hand using a digital dynamometer (predictive of functional limitation)[87]. 5. Cognitive function - Our colleagues at the FMRIB centre at Oxford University will lead the planning of **and will fund** a sub-study to test the hypothesis that a physical exercise intervention slows the rate of brain atrophy and of decline in cognitive function (see collaborative agreement). This will include using a brief battery of paper and pencil and computerised tests to assess memory, attention and executive function. We will also acquire structural and functional brain MRI measures for a sub-sample of participants, modelled on the UK Biobank Imaging extension study, to assess brain volumes, cortical thickness, white matter integrity and functional connectivity. 6. Brief measures of mental well-being (8-item Geriatric Depression Scale; energy and fatigue items from the Modified Exercise-induced Feeling Inventory [88] (6 items); the Social Well-Being scale of the Ageing Well Profile[89] (6 items)); sleep quality. 7. Health-related quality of life (EQ-5D, SF-36). 8. Activities of daily living (ADL) will be measured with the Barthel Index, which is a key measure of functional limitations used for assessing the need for and receipt of social care in the Health Survey for England.

Demographics (assessed at baseline only): BMI, deprivation index for residence (MDI), age, gender, level of education attained and ethnicity. We will compare and contrast the characteristics of people recruited to the programme with population-level data obtained from secondary sources such as the Health Survey for England 2008 and the English Longitudinal Study of Ageing. These data will also allow examination of any social patterning effects in response to the intervention.

Process Measures: 1) Intervention Fidelity: We will include a range of the strategies outlined by the NIH Behaviour Change Consortium to assess and reinforce intervention fidelity[90]. These include

checks to ensure that session delivery is compliant to treatment protocol. To maximise and monitor trial fidelity we will: (i) recruit REACT trainers with appropriate skills and experience, (ii) develop an accessible, standardised intervention manual, (iii) implement standardised REACT 'trainer training', (iv) train more REACT trainers than needed to accommodate illness or withdrawal, and (iv) monitor delivery fidelity via recording of consultation meetings for a sample of 3-4 sessions per intervention provider and the application of a 'fidelity checklist'. This approach worked well in our NIHR-funded EARS study[91] and our REACH-HF study (RP-PG-1210-12004). We will also record session attendance (intervention adherence) and relate this to outcomes. 2) Mechanisms of change A: We will use qualitative research methods to examine processes of change and elicit explanations for possible intervention success or failure. The research assistants at the three trial sites will conduct six focus group interviews with intervention participants and 6-8 individual interviews with REACT trainers. These will be conducted after a month of the maintenance stage of the intervention. Six to nine participants for each focus group will be recruited following purposive sampling to achieve diversity in ethnicity, deprivation index, gender and variance in outcomes at 6 months. A further focus group at each site will be conducted at the 24 month follow-up point to examine reasons for maintenance or non-maintenance of physical activity and physical function, with purposive sampling based on the 24 month outcomes data. Topic guides will be piloted with the service user representatives prior to use. Qualitative data will be analysed using Framework Analysis[92] based on constant comparison methods to address the research aims. Techniques to enhance the objectivity and depth of the analysis will include cross-tabulation, negative case analysis and hypothesis testing, as well as respondent validation (both in-situ and by inviting feedback on summaries of the analysed data). Service users will also be involved in the interpretation of the data through workshops to discuss transcripts and the researchers' interpretations of the data. 3) Mechanisms of change B: We will investigate the mediating and moderating effects of changes in physical activity on the primary outcome (change in physical function) and other outcomes of interest (cognitive function, sleep quality, well-being, depression) using multiple regression models. Brief questionnaires assessing mechanisms of change suggested by Social Cognitive Theory and Self-Determination Theory (the theoretical underpinnings of the intervention model) will be administered at baseline and 24 months only. A PhD studentship funded by University of Bath (see letters of support) will be dedicated to developing and implementing the REACT process evaluation.

Economic evaluation: A full economic evaluation will be undertaken to estimate the incremental cost-effectiveness of the REACT intervention compared to control i.e. incremental cost per unit of health outcome (primary outcome, QALY). We will estimate the resource use and costs for delivery of the REACT intervention, capturing the different aspects of resource use over the duration of the intervention period. Data collection/analyses will cover the three phases of the intervention (adoption, transition and maintenance), and will include set-up and training costs associated with introduction/implementation. Methods for estimating the cost for REACT will include within-trial data reporting, via trial researchers and via those delivering the intervention. The pilot phase of the proposed research will be used to finalise methods for reporting intervention-related resource use, e.g. using work-sampling methods and self-reported data. Incremental costs will be combined with data on effectiveness /health outcomes, to present a policy relevant cost-effectiveness analyses (CEA), appropriate for a range of policy makers. Primary CEA will present results against the primary outcome measure, and against cost per QALY, using a generic preference-based health status measure (EQ-5D). Given the longer term nature of potential benefits from the REACT intervention we will conduct evidence synthesis and decision-analytic modelling to assess the longer term (lifelong) consequences of the intervention versus control, including consequences in terms of health and social care costs. Analyses will follow good practice for conduct of economic evaluation in health technology assessment [97,98]. CEA will be presented to represent base case estimates (EQ-5D) and uncertainty will be considered via detailed sensitivity analyses (SF-36 [6D]). Results will include disaggregated data, as well as synthesis of cost and outcome data, and will include presentation of cost-effectiveness plane, cost-effectiveness acceptability curves, and detailed consideration of the broader impacts of the results reported.

10. Assessment and follow-up: The primary outcome and physical activity will be assessed at baseline, 6, 12 and 24 months. Other secondary outcomes will be assessed at baseline, 12, and 24 months. MRI scans will be administered at baseline and 24 months.

Assessment of harms: The definitions of the EU Directive 2001/20/EC Article 2 based on the principles of ICH Good Clinical Practice will apply. The University of Bath standard operating procedure for reporting research related Adverse Events (AEs) will be adopted. All AEs will be examined by the study medical advisor to see if they are related to the study intervention or measurement procedures. The ethics committee, the sponsor and the Data Monitoring Committee (DMEC) will be notified promptly (within 24 hours) of all Serious Adverse Events (SAEs). All AE and SAE data will be passed to the Chief Investigator who will compile a 12-monthly report for the DMEC. Adverse events will be recorded on a pro-forma and further data may accrue through patient-reporting to research staff. If a participant does not attend two consecutive sessions, they will be contacted by telephone and if the reason for non-attendance is an adverse event this will be recorded.

11. Sample size: The REACT trial will recruit a total of 768 participants across three study sites.

Effect Size: The primary aim is to assess the long-term (2 years) effect of a physical activity intervention on changes in Short Physical Performance Battery (SPPB) scores. As described above, a change of 0.5 points has been defined as representing a minimum meaningful change in SPPB score (and 1 point is considered a substantial change[30,86]). Based on data from the LIFE and LIFE-P studies, a difference between groups of 0.5 to 0.6 points in change in SPPB scores is feasible at 12 months and at 3 years [30, 93] . In the LIFE study, the standard deviation for the change in SPPB scores from baseline to 2 years was 2.2 (personal communication from J Guralnik) and in the OPAL-plus UK-based sample the SD for change in SPPB over three years was 2.0 for those with a baseline SPPB of 8 or less (our target population).

Sample Size Calculation: To detect a change of 0.5 points with a standard deviation of 2.0, assuming that loss to follow-up accumulates at 12.5% per year throughout REACT's two year follow-up period, the required sample size is 384 per arm for 85% power using two sided 5% significance. The REACT study will therefore look to recruit a total sample of 768 participants. This sample size also provides 90% power to detect a difference in moderate intensity physical activity of 50 minutes per week (SD 185 mins/wk) with 5% significance.

12. Statistical analysis: Data analysis will be undertaken blinded to group allocation. The quantitative data will be analysed and the study reported in accordance with the CONSORT guidelines for randomised controlled trials [93]. Primary comparative analyses will be on an intention-to-treat (ITT) basis with due emphasis placed on confidence intervals.

Using appropriate descriptive statistics, we will assess any imbalance between the trial arms at baseline and describe the characteristics of participants. The comparison of primary interest is the difference between the intervention and the control arm on SPPB score at the 2 year follow-up. This will be presented as between-group differences in means, 95% confidence intervals and p-values. Covariates in the model will comprise of the baseline scores and if necessary any imbalanced variables identified by the baseline analysis.

Depending on the extent of missing primary outcome data, the primary analysis will be repeated using the complete data set generated using multiple imputations. Sensitivity analyses will also be conducted to investigate the potential effects of missing data on the conclusions. Analysis of secondary outcomes will be undertaken using the same general approach as for the primary analysis, using the baseline, 1 year and 2 year follow-up data. This will include linear or logistic regression models for continuous or binary outcomes as appropriate. As a pragmatic trial of intervention effectiveness rather than efficacy, the primary ITT analysis makes no attempt to take account of actual intervention received. However, we will also investigate efficacy among participants who comply with the intervention (attending at least 67% of sessions offered) using instrumental variable methods. Further secondary analyses will explore (by entering demographic data as covariates) the

extent to which intervention effects vary with deprivation index and ethnicity. The Data Monitoring Committee will also conduct an interim analysis of effectiveness outcomes to determine whether there is a case for stopping the study early (see section 14.4). A full data analysis protocol will be developed by the trial statistician (Dr Gordon Taylor) in collaboration with the Chief Investigator and agreed with the Project Management Group and Trial Steering Committee prior to any data analysis.

13. Ethical arrangements: The Project Management Group and Trial Steering Committee will ensure that this study is conducted in full conformity with relevant regulations (ESRC research ethics framework) and with the ICH Guidelines for Good Clinical Practice (CPMP/ICH/135/95) and the Declaration of Helsinki. The protocol, informed consent form, participant information sheet and any proposed advertising material will be submitted to an appropriate Research Ethics Committee (REC) for approval within two months of REACT project commencement. The Trial Manager will be in post at the start of REACT project and will support the Chief Investigator to submit and, where necessary, obtain approval from the ethics committee for any substantial amendments to the original approved documents.

Participant Confidentiality: The trial staff will ensure that the participants' anonymity is maintained. The participants will be identified only by a participants ID number on all data collection sheets, case report forms and electronic databases. All documents will be stored securely and only accessible by trial staff and authorised personnel. Following written informed consent, participants' contact details will be stored only on encrypted computer hard drives in password-protected files. The study will comply with the Data Protection Act which requires data to be anonymised as soon as it is practical to do so.

14. Research Governance: The study will be conducted in accordance with the Research Governance Framework for Health and Social Care (2nd edition, 2005), the principles of Good Clinical Practice and the Data Protection Act, 1998. The University of Bath will act as sponsor for the trial. Four committees will be established to govern the conduct of the study: The Project Management Group (PMG), the Advisory Committee, the Trial Steering Committee (TSC) and the Data Monitoring and Ethics Committee (DMEC).

14.1. Project Management Group (PMG): The PMG will consist of the CI, all co-applicants, the trial manager, two people from our service user advisory group and the researchers at each trial centre. It will meet 4 times per year to ensure accurate implementation of the study protocol and the successful conduct and completion of the trial. The trial manager will also meet with the Chief Investigator and site leads for the three sites as needed, and each site will have its own site-specific meetings as needed to discuss day to day project management issues. In accordance with the NIHR carbon reduction guidelines[94], organisation of teleconferences will be sought for two of the four PMG meetings and SKYPE or other online communications tools will be used to minimise environmental impact.

14.2 Advisory Committee (AC): The AC will consist of our three collaborators, two service users, three services providers from our partner organisations, the CI and the trial manager. According to the Involve[95] and the NIHR PPI handbooks[96], all service users and services providers contributing to the AC will be reimbursed for their involvement. The AC will meet once a year supporting the management in refining the content of the intervention, promoting REACT with local community groups during the recruitment period, identifying dissemination channels and leading some dissemination activities contributing to the sustainability of REACT.

14.3. Trial Steering Committee (TSC): The TSC will consist of an independent Chair with expertise in ageing and public health (Prof Yoav Ben Schlomo, Bristol University), the CI, a service user representative and one other independent methodological expert to be agreed with NIHR. Representatives from the NIHR PHR programme will be invited to all TSC meetings and the trial statisticians, site PIs and health economist may be called on to attend as needed. The TSC will meet every 6-9 months from the start of the trial, providing overall supervision of the trial, monitoring trial progress and advising on scientific credibility. The TSC will consider and act, as appropriate, upon the

recommendations of the Data Monitoring and Ethics Committee (DMEC) and will have responsibility for deciding whether the trial needs to be stopped on grounds of safety or efficacy. The TSC will be blinded to all information regarding treatment assignments until the database is locked for final analysis.

14.4. Data Monitoring and Ethics Committee (DMEC): We will appoint a fully independent DMEC which will report to the TSC. This will comprise of an independent chair and an independent statistician. The CI, PIs and Chief trial statistician may be invited to attend to provide specific input by the DMEC Chair with the CI and statistician usually expected to attend the 'open session' section of the meetings. The DMEC will be responsible for the interests of the participants and its main role will be to make recommendations to the TSC as to whether the trial needs to be stopped for any ethical or safety reason (based on review of accumulating safety and outcome data). The DMEC will also plan and conduct an interim analysis of effectiveness outcomes (time point to be determined by the DMEC, but aiming to assess if a larger than expected effect size (0.4 SMD) has been achieved (in which case the study may be stopped early). To this end, the DMEC will undertake safety data reviews every 12 months after recruitment begins, unless otherwise deemed necessary. Analysed data will be blinded, unless the DMEC identifies a specific need for unblinding. A plan for interim analyses of trial effectiveness data will be established at the first meeting and agreed with the CI. Analyses will be conducted by the DMEC statistician who will be provided with a cleaned dataset by the chief trial statistician. This will include data on any adverse advents reported during the trial.

15. Project timetable and milestones:

Jan 2015: Funding confirmed. NIHR contracting / other planning processes.

1st September 2015: Official study start date: Ethics application to be submitted by end October. Co-applicants develop intervention and training manuals (to end December). Research Assistant posts advertised.

Sept-Dec 2015: Identification of facilities and REACT trainers at each site

Dec2015-Jan 2016: Training of REACT trainers.

1st Jan 2016: Researchers in post at each site.

1st Nov 2015 -end April 2016: Ethics approved. Recruit participants and baseline data collection for internal pilot study (180 people over 4 months across 3 sites) (15/site/month).

March 2016-May 2017: Deliver internal pilot study intervention with 12 months of follow-up. Intervention to be delivered to 30 people (2 groups x 15 people) per site (total 90). Qualitative and quantitative feasibility data collection. Update intervention training for each phase (adoption and maintenance) within 3-months of the end of each phase.

Sept 2016: EVALUATION OF RECRUITMENT AND RETENTION (6 month). **Decision to continue the study**

Sept 2016-May 2017: 11 months main trial recruitment period to recruit and collect baseline data for a further 578 people at 20/site/month (with 2 months leeway, allowing for 20% variation in recruitment rates).

Oct 2016 to Sept2018: 12 months intervention provision for each person recruited, with data collection for primary outcome at 6 months and data collection for all outcomes at 12 months. 24-month data collection for pilot participants.

Sept 2018 to Aug 2019: 12 months further follow-up (24-month data collection).

Sept 2019-Feb 2020: Data analysis and write-up.

29th Feb 2020: Official study end date. Total duration: 54 months

16. Expertise: Dr Stathi has led two Lifelong Health and Well-being projects on active ageing and has collaborated in several lifestyle interventions targeting older adults. She will lead the project as Chief Investigator and will be the Bath/Bristol site lead. She will lead the REACT intervention refinement and qualitative process evaluation. Dr Greaves is an associate Professor in Psychology Applied to Health and NIHR Career Development Fellow. He has been involved in the development and evaluation of 14 health behaviour interventions and in the design and implementation of 11 funded trials. He will be the Devon site lead, contribute to the REACT intervention refinement and will lead the REACT trainers' training and the quantitative process evaluation. Prof Thompson has extensive experience conducting lifestyle research and tailoring community-based studies in ethnically diverse groups in the US and UK, and will be the Birmingham site lead. She will provide expertise in cultural tailoring of the measurements and intervention. Prof Fox has broad experience in promoting physical activity in the public health arena and is a Fellow of the Faculty of Public Health. He will work with Drs Stathi and Greaves in refining the REACT intervention, developing the programme materials/manuals for REACT trainers and participants and training the REACT trainers. He will also lead the REACT Ambassadors programme. Prof Gray led the NICE Collaborating Centre for Spatial Planning and Health and brings a wealth of experience in public health research, training and delivery and has been actively involved in local NHS partnerships. Dr Taylor, Reader in health statistics has significant experience in NIHR PHR trials. He is our Chief statistician and will support the randomisation process, sample selection and oversee all the quantitative data analysis. Prof Green and Dr Medina-Lara are Health Economists with expertise in economic evaluation, modelling methods to support cost-effectiveness analyses and health outcomes, including public health analyses. They will design and conduct the economic analyses under Prof Green's supervision. Dr Bilzon is an exercise physiologist and the Director of the Disability, Sport, and Health research centre at the University of Bath. He will provide expertise in the measurement of physical limitations/mobility-related disability. Prof Johansen-Berg leads the cognitive function evaluation and will lead the fMRI sub-study which is funded by University of Oxford.

17. Partner Collaboration: Professors King and Guralnik will bring their vast experience in healthy ageing research and as co-investigators in LIFE study will assist in the refinement and evaluation of the REACT intervention content and the training materials. They will also consult the REACT team on the intervention delivery throughout the REACT study. We collaborate with BANES City Council, the Westbank charitable organisation and AGEUK Birmingham who will cover the intervention costs delivering the intervention at either their sites or in partnership with other local organisations. We will therefore involve a number of local partner organisations with a view to a) advising on and helping with recruitment and intervention delivery b) providing the facilities and staff required to deliver the intervention. At the Bristol and Bath sites, we will build on established collaborations from our OPAL, AVONet and ACE projects (including Action Age Alliance, Bristol Health Partners, LinkAge, and Golden Oldies charity). At all sites our partner organisations will include service users, public health commissioners and service providers and charity and local community organisations (a number of key people will be approached from our existing ACE Advisory Group and contacts from other previous community-based research projects) to facilitate recruitment and engagement within the targeted local communities.

At the Devon site, we have existing collaborative working relationships with the Devon County Council Health and Well-Being Board, several local leisure centres and other physical activity service providers from prior research projects, as well as several local charities and community organisations including Age Concern and the Upstream Project (a charity that engages socially isolated older people in a range of community-based activities). Our Devon partners will help us particularly in targeting rural living older people capitalising on their existing networks in rural communities.

At the Birmingham site, we will capitalise on the vast network of AGE UK and Professor Thompson's extensive network of ethnic minority groups throughout the city. Together we will identify the areas and the facilities where REACT will be delivered. The South West Peninsula Clinical Research

Network has produced service support costings for recruitment via the General Practices. Support letters from a range of the above partners have been provided.

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