NHS
Health Research Authority

REACT: REtirement in ACTion

A randomised controlled trial and economic evaluation of a community-based physical activity intervention to prevent mobility-related disability for retired older people

STUDY PROTOCOL

Version: 1.7	16th May 2018
Trial registry number and date	ISRCTN 45627165 13/06/2016
Project Reference Number:	13/164/51

Study Sponsor: University of Birmingham
Chief Investigator: Dr Afroditi Stathi (University of Birmingham)

This protocol has regard for the HRA guidance and order of content

Health Research Authority

FULL TITLE OF THE TRIAL

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

SHORT STUDY TITLE / ACRONYM	REACT: REtirement in ACTion
PROTOCOL VERSION V 1.7	**1**6/05/18
IRAS Number:	169691
ISRCTN Number:	45627165

SIGNATURE PAGE

The undersigned confirm that the following protocol has been agreed and accepted and that the Chief Investigator agrees to conduct the trial in compliance with the approved protocol, GCP guidelines and the Sponsor's SOPs.

I agree to ensure that the confidential information contained in this document will not be used for any other purpose other than the evaluation or conduct of the clinical investigation without the prior written consent of the Sponsor

I also confirm that I will make the findings of the study publically available through publication or other dissemination tools without any unnecessary delay and that an honest accurate and transparent account of the study will be given; and that any discrepancies from the study as planned in this protocol will be explained.

For and on behalf of the Study Sponsor:

Signature: Date: 16/05/2018

.....

Name: Dr Sean Jennings .....

Position: Research Governance and Ethics Manager…….....

Chief Investigator:

Signature: Date: 11/11/2015.

....

Name: Dr Afroditi Stathi.....

Statistician:

Signature:

Date: 11/11/2015.

.....

Name: (please print):

Dr Gordon Taylor.....

Position:

REACT Chief Statistician .....

KEY TRIAL CONTACTS

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Sponsor	University of Birmingham Edgbaston B15 2TT
Joint-sponsor(s)/co-sponsor(s)	None.
Funder(s)	National Institute for Health Research - Public Health Research programme Bath and North East Somerset Council Denice Burton, Assistant Director – Health Improvement St Martin's Hospital, Clara Cross Lane, Bath BA2 5RP denice_burton@bathnes.gov.uk Tel 01225 394061 Westbank Jaine Keable, Head of Health and Wellbeing Farm House Rise, Exminster, Exeter EX6 8AT Tel 01392 824752 AGE UK Birmingham Ms. C. Hayward, Chief Executive Officer 55 Alcester Road South, Kings Heath Birmingham B14 7JG info@ageukbirmingham.org.uk Tel 0121 4370033 University of Oxford (fMRI imaging sub-study) Professor Heidi Johansen-Berg FMRIB Centre, John Radcliffe Hospital, Headington, Oxford, OX3 9DU heidi@fmrib.ox.ac.uk Tel01865 222548 University of Bath (PhD Scholarship) Professor Jonathan Knight, Pro-Vice-Chancellor for Research Claverton Down, Bath BA2 7AY Pro-vc-research@bath.ac.uk Tel 01225 386141
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Committees	**Trial Steering Group** Chair Professor Yoav Ben-Shlomo Tel 0117 9287206 Email y.ben-shlomo@bris.ac.uk **Data Monitoring Committee**

	Chair Professor Dawn Skelton Tel 01413318792 Email: dawn.skelton@gcu.ac.uk **Trial Management Group** Chair Dr Afroditi Stathi Tel: 0121 415 8389 Email a.stathi@bham.ac.uk

TRIAL SUMMARY

Trial Title	**REACT: REtirement in ACTion. A randomised controlled trial and economic evaluation of a community-based physical activity intervention to prevent mobility-related disability for retired older people**	
Internal ref. no. (or short title)	REACT: Retirement in ACTion	
Research sites	Bath/Bristol, Birmingham and Devon	
Trial Design	REACT is a multi-centre pragmatic two-arm parallel-group randomised controlled trial with an internal pilot phase	
Trial Participants	Men and women aged 65 or older, not in full-time work, with declining physical function, defined as scoring 4-9 (inclusive) on the Short Physical Performance Battery (SPPB), who are planning to reside in the target area (Bath/Bristol, Devon, Birmingham) for at least 24 months.	
Planned Sample Size	Total of 768 participants across all three trial sites	
Intervention duration	12 months	
Follow up duration	24 months	
Planned Trial Period	Internal pilot Recruitment commences January 2016 Intervention delivered March 2016 - May 2017 Full trial Recruitment commences September 2016 Intervention delivered October 2016 – August 2018	
	Objectives	Outcome Measures
Primary	To assess the 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.	The primary outcome will be the Short Physical Performance Battery (SPPB) score at 24 months. SPPB assesses lower limb function in terms of observed ability to complete a repeated sit-to-stand task, a standing balance test and a gait speed assessment.
Secondary	To test the hypotheses that: 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, ability to perform the activities of daily living, mental and social well-being and have reduced pain and improved	Minutes of moderate intensity physical activity, as measured by wrist-worn accelerometers Sedentary time and breaks in sedentary time per day assessed by wrist-worn accelerometers. Self-reported physical activity (PASE questionnaire) Hand grip strength of the dominant hand using a digital dynamometer.

	sleep quality at 24 months. In addition a full economic evaluation will estimate the incremental cost-effectiveness of the REACT intervention.	Ageing Well Profile Social scale (6 items) Activities of daily living (ADL) (EQ-5D, SF-36, MAT-sf) The UK Biobank Healthy Minds Questionnaire (memory, attention and executive function) The incremental cost-effectiveness of the REACT intervention (EQ-5D, SF-36) Pain (Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) Sleep Condition Indicator Medical history Falls Inventory Health and Social Service Usage Process Evaluation Exercise Adherence rating scale Attitudes to and experience of physical activity (PA) Keeping track of PA Feedback on REACT Co-interventions and health changes *fMRI imaging sub-study* Rate of brain atrophy and decline in cognitive function (fMRI scan) and battery of computerised cognitive tests. Gait analysis

FUNDING AND SUPPORT IN KIND

FUNDER(S) (Names and contact details of ALL organisations providing funding and/or support in kind for this trial)	**FINANCIAL AND NON FINANCIALSUPPORT GIVEN**
National Institute for Health Research - Public Health Research programme	£1,641,796.80
Bath and North East Somerset Council Denice Burton, Assistant Director – Health Improvement St Martin's Hospital, Clara Cross Lane, Bath BA2 5RP denice_burton@bathnes.gov.uk Tel 01225 394061	Financial support: £35,000 Non-financial support: Recruitment support
St Monica Trust Donna MCDermott Cote Lane, Westbury-on-Trym Bristol BS9 3UN 0117 9494000	Non-financial support: Provision of session venues, session leaders and recruitment support
Westbank Jaine Keable, Head of Health and Wellbeing Farm House Rise, Exminster, Exeter EX6 8AT Tel 01392 824752	Non-financial support: Provision of session venues, session leaders and recruitment support
AGE UK Birmingham Ms. C. Hayward, Chief Executive Officer 55 Alcester Road South, Kings Heath Birmingham B14 7JG info@ageukbirmingham.org.uk Tel 0121 4370033	Non-financial support: Provision of session venues, session leaders and recruitment support
University of Oxford Professor Heidi Johansen-Berg FMRIB Centre, John Radcliffe Hospital, Headington, Oxford, OX3 9DU heidi@fmrib.ox.ac.uk Tel01865 222548	fMRI Imaging sub-study Financial support £220,000
University of Bath Professor Jonathan Knight, Pro-Vice-Chancellor for Research Claverton Down, Bath BA2 7AY Pro-vc-research@bath.ac.uk Tel 01225 386141	Financial support: £56,970 Award of one PhD Scholarship to support the REACT process evaluation
Bristol Ageing Better fund	£4,972 to run REACT sessions in Easton, Bristol

ROLE OF STUDY SPONSOR AND FUNDER

The University of Birmingham will act as sponsor for the trial. The Chief Investigator and Trial Manager are employees of the University of Birmingham and Bath respectively and will oversee the trial design, conduct, data analysis and interpretation, manuscript writing, and dissemination of results.

REACT is funded by the National Institute for Health Research - Public Health Research Programme. The funder expects the research team to conduct the study according to the trial as described and as set in the NHS ethics application. NIHR has the right to publish itself any non-confidential material generated from this project. NIHR will however consult with the PI if this is to occur.

ROLES AND RESPONSIBILITIES OF TRIAL MANAGEMENT COMMITEES/GROUPS & INDIVIDUALS

Trial Management Committees

- Trial Steering Committee

  The TSC will consist of an independent Chair with expertise in ageing and public health (Prof Yoav Ben-Shlomo, Bristol University); the CI; a service user representative, Dr Paul Bennett, an independent medical advisor, Professor Peter Thomas, an independent statistician from the University of Bournemouth; Professor Diane Crone of the University of Gloucestershire, an expert in the design, delivery and evaluation of health promoting interventions in primary care and in the community; Jameelah Ingram, a public health expert from Bath and North East Somerset Council and Dr Kate Walters, Director of the Centre for Ageing & Population Studies at UCL an expert in complex interventions in primary care and community settings. 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 or if the DMEC recommends that results need to be reviewed.

- Data Monitoring and Ethics Committee

  A fully independent DMEC has been appointed which will report to the TSC. This will comprise of an independent chair Professor Dawn Skelton (Glasgow Caledonian University), Professor Paul Ewings, the Director of NIHR Research Design Service South West and Professor Kamlesh Khunti, Professor in Primary Care (University of Leicester). 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 data). The DMEC will undertake safety data reviews every 12 months after recruitment begins, unless otherwise deemed necessary. This will include data on any adverse advents reported during the trial. Analysed data will be blinded, unless the DMEC identifies a specific need for unblinding.

- Trial Management Group

  The TMG 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 to discuss day to day project management issues. In accordance with the NIHR carbon reduction guidelines,

organisation of teleconferences will be sought for two of the four TMG meetings and SKYPE or other online communications tools will be used to minimise environmental impact.

Protocol contributors

The protocol was prepared by Dr Afroditi Stathi, Chief Investigator (University of Birmingham) and Dr Janet Withall, REACT Trial Manager (University of Bath). The statistical analysis was prepared by Dr Gordon Taylor (University of Exeter) and Dr Sean Williams (University of Bath) and the economic evaluation by Dr Antonieta Medina-Lara (University of Exeter). Professor Heidi Johansen-Berg (University of Oxford) contributed all elements relating to the fMRI imaging sub-study.

The funder (NIHR) expects the research team to conduct the study according to the trial as described and as set out in the NHS ethics application and took no part in the development of the protocol.

PPI involvement

REACT 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. Our Avon Network for the Promotion of Active Ageing in the Community (AVONet) (MRC Lifelong Health and Wellbeing – Collaborative Development Network (Ref 90543)) used 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. The REACT study was considered by our AVONet service user, service provider and commissioner stakeholders to be suitable for delivery across a range of socio-economic and cultural populations. The REACT protocol has been developed based on this input. The Trial Management Group was closely involved in the development of the study protocol and three people from our service user advisory group (research partners) form part of that committee. The Trial Steering Committee which approved the protocol prior to submission included a service user representative. In addition the draft protocol was open to consultation by our service user representatives, our public health expert and members of community organisations.

KEY WORDS: Physical activity, disability prevention, older adults, randomised control trial, mobility disability, physical function

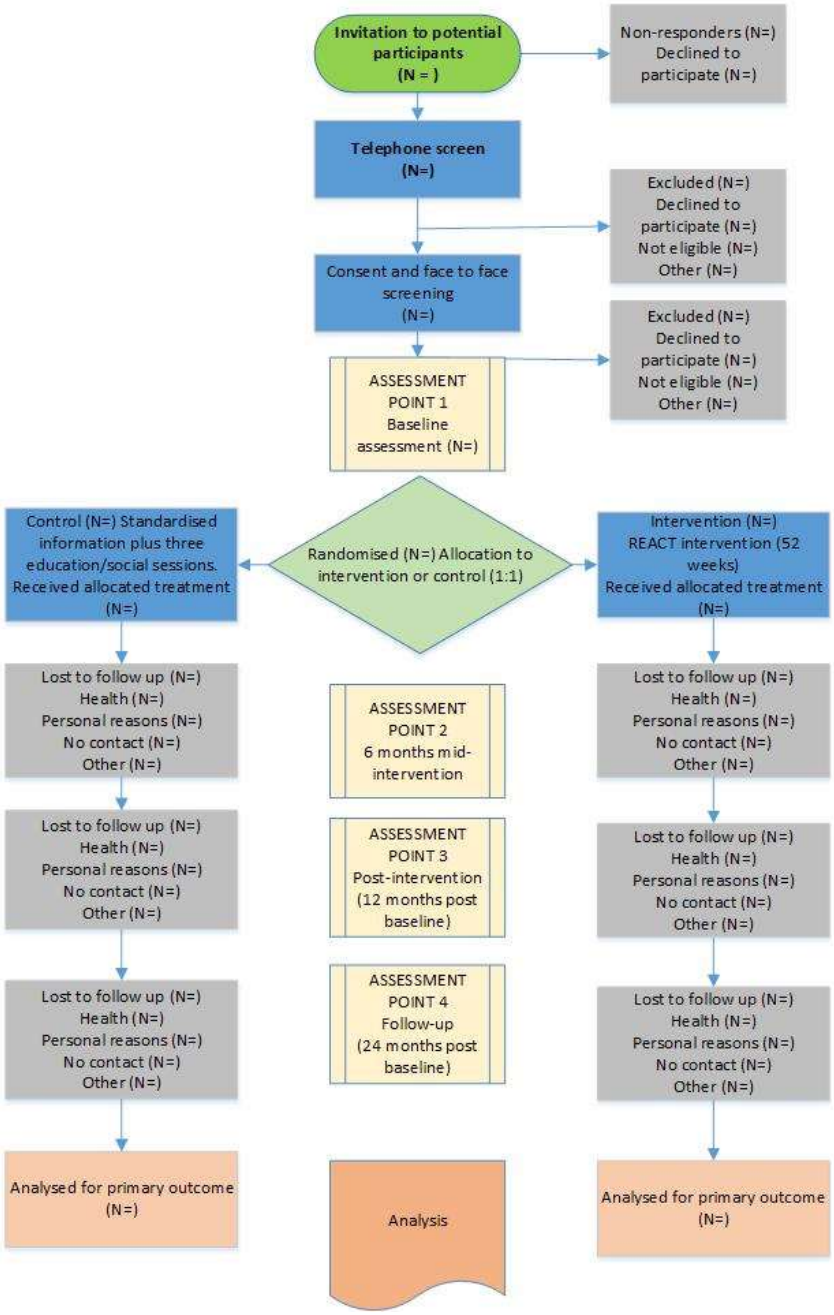
LIST of CONTENTS

LIST OF ABBREVIATIONS

Define all unusual or 'technical' terms related to the trial. Add or delete as appropriate to your trial. Maintain alphabetical order for ease of reference.

AE	Adverse Event
CI	Chief Investigator
CRF	Case Report Form
DMEC	Data Monitoring and Ethics Committee
EC	European Commission
EU	European Union
EUCTD	European Clinical Trials Directive
EudraCT	European Clinical Trials Database
GCP	Good Clinical Practice
IB	Investigator Brochure
ICF	Informed Consent Form
IDMC	Independent Data Monitoring Committee
ISF	Investigator Site File
ISRCTN	International Standard Randomised Controlled Trials Number
NHS R&D	National Health Service Research & Development
PI	Principal Investigator
PIC	Participant Identification Centre
PIS	Participant Information Sheet
QALY	Quality-Adjusted Life Year
RCT	Randomised Control Trial
REC	Research Ethics Committee
SAE	Serious Adverse Event
SDV	Source Data Verification
SOP	Standard Operating Procedure
SSI	Site Specific Information
TMG	Trial Management Group
TSC	Trial Steering Committee
TMF	Trial Master File

REACT Participant Flow



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

1 BACKGROUND

Review of relevant studies

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 and social 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].

The LIFE clinical trial

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 study utilised an active control group which 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 administered in a real world setting and tailored for a UK population of older adults who are at risk of losing functional mobility.

Description of the REACT Intervention

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 and promote long-term compliance.

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 (See Appendix 1).

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, plus 15-20 minutes 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 (See Appendix 2). 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, in the neighbourhood or at a local physical activity session. 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 while continuing with a weekly centre-based physical activity session followed by a short social session. Participants will enact action plans that were made during the transition phase and will be supported through group social/education meetings once a month. At this stage we may 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 taster activity sessions (supplied by our collaborators and partners, other local service providers /companies, including health walks, 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 (See Appendix 1). 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. For details of sample physical activity sessions see Appendix 4. 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.

Control Arm: After completion of baseline assessments, participants allocated to the control group will be given information regarding events and activities in their local community. They 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 the completion of the six month assessment, control participants will be invited to a further 60-minute group social/education session. Between the 12 and 24-month data collection sessions, controls will be invited to a further 60-minute group session (See Appendix 2 for details). After 24-month data collection, controls 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.

Description of the REACT population

REACT will recruit sedentary, community living, older persons aged 65 and over, with functional limitations (i.e. who are at risk of major mobility limitations), but who are still ambulatory, i.e. they can still walk. This will be measured using a physical function test (SPPB) which uses three simple tests to access balance, walking speed and the ability to go from a sitting to a standing position. Older adults with scores of 4-9 (inclusive) out of 12 will be eligible to take part in REACT. The aim is to target a non-disabled, but at-risk population. REACT will be delivered in Bristol/Bath, Birmingham and Devon and will target areas for recruitment that represent a broad range of socio-economic status. The target number of participants is 768 across the three centres.

2 RATIONALE

REACT 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.

REACT secondary hypothesis

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, ability to perform the activities of daily living, mental and social well-being and have reduced pain and improved sleep quality at 24 months.

Trial justification

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.

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.

2.1 Assessment and management of risk

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 REACT trainers will be qualified to at least Level 3 (Exercise Referral Diploma or equivalent).

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]. Engaging in any kind of group activity facilitates social interaction and helps address social isolation which has itself been shown to positively impact physical and mental health in addition to improving quality of life.

A preliminary phone screening will exclude participants who have unstable or uncontrolled cardiovascular or musculoskeletal health issues, a diagnosis of dementia or serious mental illness.

Participants will be asked to consent to allowing the research team to contact their GP if any concerns about their health or well-being arise.

The Trial Steering Committee and the Data Monitoring and Ethics Committee will oversee all patient safety issues, which the REACT independent medical advisor, Dr Paul Bennett, will review in detail

The University of Birmingham standard operating procedure for reporting research related Adverse Events (AEs) will be adopted. The detailed process for the reporting of Adverse Events and Reactions is outlined in the REACT study protocol and the IRAS submission. The DMEC will monitor and analyse data on any adverse events reported during the trial.

3 OBJECTIVES AND OUTCOME MEASURES/ENDPOINTS

3.1 Primary objective

Primary research question

What is the effectiveness and cost-effectiveness, compared with a minimal intervention control condition, of a community-based physical activity intervention (REACT) for reducing the progression of functional limitations in older people who are at high risk of mobility related disability?

Primary 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.

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.

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.

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

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.

3.2 Secondary objectives

1. To compare minutes of moderate intensity physical activity, as measured by accelerometer data, between intervention and control groups

2. To compare sedentary time and breaks in sedentary time between intervention and control groups.

3. To compare self-reported physical activity between intervention and control groups.

4. To compare hand grip strength of the dominant hand between intervention and control groups.

5. To compare performance on a brief test of cognitive function between intervention and control groups.

6. To compare the rate of brain atrophy and performance on more detailed tests of cognitive function and gait analysis tests between intervention and control groups (fMRI imaging sub-study).

7. To compare mental and social well-being, energy, sleep quality and pain between intervention and control groups.

8. To compare health-related quality of life between intervention and control groups.

9. To compare activities of daily living (ADL) scores between intervention and control groups.

10. To conduct a full economic evaluation to estimate the incremental cost-effectiveness of the REACT intervention compared to control i.e. incremental cost per unit of health outcome.

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, ability to perform the activities of daily living, mental and social well-being at 24 months.

3.3 Primary endpoint/outcome

Primary Outcomes

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].

3.4 Secondary endpoints/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 (ommon problems with waist worn accelerometers).

2. Sedentary time and breaks in sedentary time per day assessed by accelerometry.

3. Self-reported physical activity (PASE questionnaire)[53] . 4. Hand grip strength of the dominant hand using a digital dynamometer (predictive of functional limitation)[87].

5. Brief measures of mental well-being the Social Well-Being scale of the Ageing Well Profile[89] (6 items));Sleep Condition Indicator[88] (8 item) pain (Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) (5 item).

6. Health-related quality of life (EQ-5D, SF-36).

7. Activities of daily living (ADL) will be measured with the Mobility assessment tool-short form (MAT-sf (See Appendix 5)), SF36 and EQ-5D.

8. Medical history, Falls Inventory and Health and Social Service Usage

9. Cognitive function will be measured using the UK Biobank Healthy Minds Questionnaire which assesses memory, attention and executive function

10. Cognitive function – *(fMRI imaging substudy).* Our colleagues at Oxford University will test the hypothesis that a physical exercise intervention slows the rate of brain atrophy and of decline in cognitive function. Measures include a brief battery of paper and pencil and computerised tests to assess memory, attention and executive function; structural and functional brain MRI measures and gait analysis for a sub-sample of participants.

11. The cost-effectiveness analysis will present results against the primary outcome measure, and against cost per QALY, using a generic preference-based health status measure (EQ-5D) for base case estimates and uncertainty will be considered via detailed sensitivity analyses using the (SF-36).

As part of the REACT process evaluation brief questionnaires, interviews and focus groups will be administered. For full details of the Process Evaluation see Appendix 10.

The REACT intervention will be delivered by partner organisations. Some of these organisations mayl require the completion of their own evaluation questionnaires. Subject to ethical approval these documents will be circulated to REACT participants with their allocation letter (with a reply paid envelope) at baseline and by post at other time points requested by partner organisations.

4 TRIAL DESIGN

The REACT study is a multi-centre pragmatic two-arm parallel-group randomised controlled trial with 1:1 individual participant allocation to the REACT intervention or a minimal intervention control condition. REACT will incorporate an internal pilot phase and nested process and economic evaluations. Following identification and recruitment, 768 patients who meet the study inclusion criteria will be randomised to receive either the REACT intervention, delivered over a period of 12 months by trained intervention facilitators or a minimal control intervention.

Outcome data will be collected at baseline, 6, 12 and 24 months.

Stopping rules or discontinuation criteria

The Trial Steering Committee, with advice from the Data Monitoring and Ethics Committee, will assess the feasibility of the trial 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 equivalent of 1FTE 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). After 6 months, recruitment data will be reviewed by the TSC and any required changes in the recruitment strategy and/or introduction of new recruitment avenues will be discussed and agreed. Retention rates (proportion of people providing follow up data) will also be checked at 6 months. Receipt of strong negative feedback from the majority of either participants or intervention providers about the intervention or trial methods will be considered as a stopping criterion. The participants recruited in the pilot study will be included in the trial analysis.

5 STUDY SETTING

Trial sites

REACT will be conducted at three trial sites in Bath/Bristol, Devon, and Birmingham, allowing recruitment of a socio-economically diverse sample including ethnic minorities, and participants from urban, rural and semi-rural locations. Conduct of the trial at each site will be led by a local Principal Investigator supported by a Research Assistant who will receive training in the requirements of the study protocol.

Intervention Setting

The REACT intervention will be conducted at leisure/community centres and fitness/health clubs provided by, or funded by, REACT collaborators during low usage hours in economically and ethnically diverse areas of Bath/Bristol, Devon, and Birmingham.

Session delivery

All sessions will be led by professionals trained to deliver exercise for older adults in a safe manner. REACT trainers will be qualified to at least Level 3 (Exercise Referral Diploma or equivalent) and will be experienced in delivering exercise sessions to older adults. They will receive specific training in delivering the REACT sessions. Dr Greaves will lead the REACT trainers' training and will work with Professor Fox and Dr Stathi to develop the trainers' programme materials and manuals.

6 ELIGIBILITY CRITERIA

6.1 Inclusion criteria

- Men and women aged 65 or older who are not in full-time employment
- Planning to reside in the target area (Bath/Bristol, Devon, Birmingham) for at least 24 months
- Participants must score between 4 and 9 (inclusive) on the Short Physical Performance Battery (SPPB)[54]. This is based on data showing that older adults with SPPB scores of 9 or less have substantially higher risk of major mobility disability three years later (OR = 8.3 (95%CI: 3.3 to 20.67) compared with those who score 12 [30,52]. Our data from the OPAL study show that 38% (90/240) of recruited UK adults over 70 scored 9 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 30% 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 or recruitment procedures need refinement (e.g. if they lead to over-exclusion of participants).

6.2 Exclusion criteria

- A documented or patient-reported medical condition that would preclude participation, including arthritis so severe it would prevent participation in physical activity, Parkinson's disease, dementia; any terminal illness, lung disease requiring use of corticosteroids or supplemental oxygen, severe kidney disease that requires dialysis; severe heart disease that would prevent participation in physical activity (for example chest pain when walking one or two hundred yards or up a flight of stairs); an implanted cardiac defibrillator, a cardiac arrest which required resuscitation; severe uncontrolled psychiatric illness; currently receiving radiation therapy or chemotherapy treatment for cancer; awaiting knee or hip surgery, major heart surgery (including valve replacement or bypass surgery) or spinal surgery in the last six months or any other clinical condition that their GP or clinician considers would make them unsuitable for participation in a physical activity rehabilitation programme to prevent decline of lower-limb functioning.
- Self-reported inability to walk across a room or the need for a walker or the help of another person;
- Existing major mobility limitation. This will be defined using a SPPB lower cut-off score of 3 or less). 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 (see above);
- Living in residential or nursing care

For fMRI imaging sub-study:

- Contraindications for MRI scanning (assessed using CRICBristol SOP Screening Subjects for Safety to Scan)
- History of neurological illness (e.g. stroke)
- Current treatment for a psychiatric illness
- Insufficient English to understand what participation entails and provide consent in English

7 TRIAL PROCEDURES

For Trial Project Management Plan see Appendix 6

Sept – Dec 2015: Study set-up

Nov 2015: Ethics submission

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

Oct-Nov 2015: Research Assistants' recruitment

Oct-Dec 2015: Preparing training manual for REACT specialists

Nov 2015 – Jan 2016 Identify partner GP practices and set up recruitment processes

Dec 2015-Jan 2016: Training of REACT specialists

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

13th Jan 2016: REACT launch event

Jan – Apr 2016: INTERNAL PILOT- Recruitment
(60 people per site) x 3 sites =180 people in total for internal pilot (90 intervention-90 control)

Feb – May 2016: INTERNAL PILOT- Baseline measures
180 participants: 60 at each site

Feb – May 2016: INTERNAL PILOT- Adoption phase (12 weeks)
90 intervention participants: 30 at each site (2 groups of 15)

June 2016 – May 2017: INTERNAL PILOT- Maintenance phase (40 weeks)
90 intervention participants: 30 at each site (2 groups of 15)

Dec 2016: EVALUATION OF PILOT AND DECISION TO CONTINUE TO MAIN TRIAL

Sept 2016 – June 2017: MAIN TRIAL- Recruitment
(768 sample size and 180 recruited for the pilot)=588 remaining participants to be recruited)

20/per site/per month (with two months leeway, allowing for 20% variation in recruitment) 60 per month= 10 months for recruitment

Sept 2016 – June 2017: MAIN TRIAL - Baseline measures

Oct 2016 – July 2017: MAIN TRIAL - Adoption phase (12 weeks)
Intervention participants (588/2=294 participants). 98 per site. 7 groups per site.

Jan 2017 – Aug 2018: MAIN TRIAL - Maintenance phase (40 weeks)
Intervention participants (588/2=294 participants). 98 per site. 7 groups per site.

Feb – April 2017 INTERNAL PILOT 12 month follow-up data

Sept 2017 – Aug 2018 MAIN TRIAL – 12 month follow-up data

Feb - April 2018 INTERNAL PILOT 24 month follow-up data

Sept 2018 – Aug 2019 MAIN TRIAL – 24 month follow-up data

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

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

7.1 Recruitment

The goal of the study is to enrol 768 participants across the 3 trial sites, Bristol/Bath, Birmingham and Devon.

All recruitment related activities will be overseen by the CI, Trial Manager and Trial Management Group. The Trial Manager will coordinate press and media releases and assist the sites in the preparation of recruitment materials.

Each trial site will develop a site-specific recruitment plan built around four main strategies to accommodate the variability across centres in catchment area characteristics and routes to access potential participants. All recruitment materials will be reviewed by the appropriate PI before being used.

7.1.1 Patient identification

REACT will use three main recruitment strategies:

1) Via Primary Care
2) Via Third Sector organisations
3) Word-of-mouth and snowball sampling techniques with the assistance of bi-lingual community champions (via existing community contacts).

These recruitment approaches will be supported by a low cost public relations campaign targeting local newspapers, magazines, radio and community events (See Appendix 7). We will work closely with our collaborators, local community groups, charities and the public sector, using their existing networks to leverage our recruitment process. 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 (See Appendix 8). We will also use 'word-of-mouth' by encouraging potential participants to pass information to others who may be eligible.

Via Primary Care

Recruitment of GP practices

General practitioner (GP) Practices in the Clinical Commissioning Groups will be invited to participate through their local Clinical Research Network (CRN) and through existing networks. Where possible we will select practices to maximise diversity in terms of ethnicity socio-economic status and (in Devon) rurality. Practices who agree to participate will be contacted by a member of the local research team (PI,Trial Manager or RA) for an appointment with the practice manager or IT administrator to arrange to meet, discuss the study and conduct a database search.

GP register search

Practice staff will search for potentially eligible patients using the trial entry criteria. Where possible (if there are more potential participants then we need to write to) we will seek to maximise diversity (by stratification) in terms of age and postcode. Searches will be tailored to individual practice procedures. We will also explore other risk stratification tools to identify most efficiently the sample we wish to contact. Lists generated from the searches will be further screened for suitability by a GP at each practice.

Search details:

1) All people aged 65 years and older
2) Where possible using search codes: Exclude people with a) arthritis so severe it would prevent participation in physical activity, b) Parkinson's disease, c) dementia; d) lung disease requiring use of corticosteroids or supplemental oxygen, e) severe kidney disease that requires dialysis; f) severe heart disease that would prevent participation in physical activity; g) an implanted cardiac defibrillator, h) a cardiac arrest which required resuscitation; i) severe uncontrolled psychiatric illness; j) currently receiving radiation therapy or chemotherapy treatment for cancer; k) awaiting knee or hip surgery, l) major heart surgery or spinal surgery in the last 6 months m) using a wheelchair or Zimmer frame n) terminal illness o) living in residential care or nursing home. NB: if the field for any of the above exclusion criteria is not completed, the assumption should be that the exclusion does not apply (only a positive recorded event or condition should result in exclusion).
3) GP or his /her appointed representative to review the list to a) check the above exclusions do not apply b) exclude anyone with any of the above criteria that cannot be searched for, c) exclude anyone who is known to already have a major mobility limitation (being unable to walk 4 metres or being unable to do this without a Zimmer frame or support from another person - using a walking stick is OK) and d) exclude anyone with any other clinical condition that their GP considers would make them unsuitable for participation in a physical activity rehabilitation programme to prevent decline of lower-limb functioning.

Patient Approach letter
A Patient Approach letter (and the reply form and the Participant Information Sheet (PIS)) printed on the Practice headed notepaper will be sent to suitable patients, enclosing a reply-paid envelope addressed to the research team at the local trial site. The letter will make it clear that we wish to recruit people who have some difficulty doing daily activities such as walking, getting out of a chair, and climbing stairs but are still able to do these things. This constitutes the first phase of the screening process – Initial self-screening (see more details below). Patients will be asked to return the reply form to the research team if they feel they meet the study criteria and are interested in talking to a member of the research team about the study. If the target recruitment rate is not achieved general practices will be asked to send out follow-up approach letters to the same patients 14-21 days. The follow-up approach letters will include an acknowledgement that the follow-up letter may be ignored by those patients who have responded to the initial letter. GPs and practice nurses could also be asked to offer the recruitment pack in surgery to patients they consider would fit the REACT recruitment criteria.

Via Third Sector organisations
PIs at each trial site will also be responsible for engaging with third sector and community based organisations who engage with adults over 65 years old (e.g. Age UK, Brunelcare, St Monica's Trust, LinkAGE, Contact the Elderly etc.) Professionals in these services will approach potentially eligible service users and provide a brief summary of the study, followed by provision of the Participant Approach letter and PIS (if deemed appropriate), or they may post the Participant Approach letter, PIS and reply form to service users instead with a reply-paid envelope addressed to the research team at the local trial site. In addition, opportunities for the PI or site RA to present REACT to gatherings of service users will be sought. This will only be done in the presence of the host organisation's staff. Any service user expressing an interest will be provided with the Participant Approach letter, PIS and reply-paid form (if deemed appropriate).

Via word-of-mouth and snowball sampling techniques
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 can be more effective for recruiting ethnic minorities than recruiting via healthcare professionals. The local PI or RA will work closely with community champions already known to the research team to identify ethnic minority groups or individuals who may meet the REACT inclusion criteria. The initial approach would be made by the community champion who would provide a brief summary of the study, followed by provision of the Participant Approach letter, reply form, PIS and reply-paid envelope (if deemed appropriate). This material would be translated where necessary.

Recruitment response rates

To achieve the desired levels of recruitment (768) we estimate that we would need to contact 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 initial letter/contact 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.

The overall response rate based on the number of people contacted who end up taking part is estimated to be 8.5%. The number of people who are eligible within the over 65 population is

estimated at 200 per thousand. The number of people who are eligible within the total general practice population (all ages) is estimated at 43 per thousand (based on 21.3% of people in Devon being aged over 65 as an example). The number of people who are likely to take part (based on the above assumptions) is 3.6 per thousand. (Hence to recruit 256 people at each site, we need to recruit from a total population (i.e. membership of practices or other recruitment centres) at each site of 71,000 people). In the pilot stage, to recruit 30 people at each site, we need practices or other centres with total population of at least 8350.

Recruitment Monitoring and Assistance

Participants arising from all methods of recruitment will be documented by each of the REACT trial centres by means of coded reply slips. In addition, during the telephone screening interview, potential participants will be asked about where they heard about the study. These data are used to generate regular reports through the whole recruitment period to track the method(s) that provide the greatest yield of eligible participants. These reports will be provided to the Trial Manager on a weekly basis and to the Trial Management Group members on a bi-monthly basis and provide data on the number of potential participants screened from each of the recruitment sources, eligible participants from the various recruitment sources, and eligible ethnically diverse participants from the recruitment sources. 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.

Initial response

Older adults who are interested in participation based on the initial invitation will instigate contact with the research team by returning the approach letter reply slips. Patient and Participant Approach letters and reply slips will undergo Research Ethics Committee review and approval prior to use.

Provision of study information

Once an approach letter reply slip has been received from a potential participant, an RA will telephone the patient using the contact details provided by the patient on the reply form. The telephone call will be used by the research team member to provide further information to the patient if necessary, to confirm ongoing willingness and to conduct the second, phone based phase of the screening process. If the call establishes that the patient is potentially eligible and willing to participate arrangements will be made for them to attend a baseline recruitment session. Transport to this session can be offered.

Recruiting for Diversity

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 and diversity utilising our established links with community groups, faith leaders, and GP surgeries that serve ethnically and economically diverse communities. 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 the pilot study shows that the recruited sample is not broadly representative of the UK population.

Each REACT trial site will track recruitment methods to determine the most successful strategy for recruiting minority groups in order to ensure socio-economic diversity amongst the cohort.

Translation

In order to maximise recruitment and retention from ethnically diverse populations, interpreters will be provided at key points in the study. Using an approach employed successfully in the Community-based Prevention for Diabetes (ComPoD) trial, the Patient Approach letter will contain a tick box inviting potential participants to inform the research team if they would need an interpreter in order to participate in REACT, and if so in what language. For these participants, telephone screening will be conducted by an interpreter using the screening script, with oversight provided by the site-based Research Assistant. Interpreters will also translate at the point of consent and scheduling of data collection events, during the SPPB, grip strength tests, and delivery of the activity monitors, at the face-to-face screening and at baseline, 6 months, 12 months and 24 month data collection events. Interpreters will deliver the questionnaire-based data collection at the same time points. Interpreters will also translate at the first two exercise sessions and the first two social/educational sessions attended by any non-English speaking participants. These interpreters will be recruited from our established links with local interpreter services via the University of Birmingham and NHS, and we will provide additional training of interpreters to assist with data collection as needed.

Recruitment launch event

At the beginning of the recruitment process, we will hold a one 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 evaluated during the internal pilot stage and any necessary changes on recruitment and sampling framework will be discussed, identified and agreed by the Trial Management Group and Trial Steering Committee prior to the start of the main phase of the study.

Retention

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-based 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, actively building social networks, the Ambassador's programme and supporting the engagement of participants in community activities.

7.1.2 Screening

The eligibility of respondents will be assessed in a three-step sequential screening process:-

1. Initial self-selection: The Patient/Participant Approach letters, PIS and the Study invitation letters will make it clear that we wish to recruit people who have some difficulty doing daily activities such as walking, climbing stairs and getting out of a chair but 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 (PIS) will have been posted to people with the invitation letter, and a preliminary phone screen will check inclusion and exclusion criteria that can be assessed by phone (e.g. self-reported inability to walk across a room). Participants who do not meet

the eligibility criteria will be thanked for their time and mailed an information pack including advice on physical activity, sources of advice and information and details of appropriate local activities.

3. Face to face screening sessions: Potentially eligible participants will then be invited to a group-based assessment session. This method involves having several 'stations' for each step in the assessment 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) (See Section 7.2). They will then be administered the SPPB in a private room. The gait speed test will be conducted first and those who fail to complete the 4 metre walk will be screened out of the study and will not continue to the other SPPB tests. Participants who meet the eligibility criteria will be invited to complete the remainder of the baseline assessments. As above, participants who do not meet the eligibility criteria will be thanked for their time and provided with an information pack.

4. fMRI Imaging sub-study: REACT participants who have consented to discuss participation in the fMRI Imaging sub-study will be screened by telephone using the CRICBristol SOP Screening Subjects for Safety to Scan. This will be repeated immediately before the MRI scan.

7.2 Consent

Older adults who are willing to take part in REACT will be asked to provide verbal informed consent at the beginning of the telephone screening call and written informed consent prior to commencement of the face-to-face screening sessions.

Consents to be Obtained

1) Verbal consent

The REACT trial has two informed consent forms: one verbal and one written. The verbal consent is read prior to the beginning of the phone screening interview. If the participant fails to give consent, then a phone screen will not be done. If a participant provides verbal consent, then the assignment of a study ID number will be taken as positive evidence that initial consent was obtained.
The Phone Screening form may be administered as a face-to-face interview if the situation warrants it.

2) Written Consent

The Environment for Consent

The setting in which written consent is obtained at the face to face screening session will be as private as possible so that participants can freely ask questions without embarrassment. To avoid pressuring the participant, only one person associated with the study will be present when the participant reviews the consent forms.

The Consent process

The consent process will involve a full explanation of the study given by the person taking consent (RA or other authorised researcher) prior to any of the face-to-face screening processes commencing. Potential participants will be informed that they may, at any time, withdraw their consent to participate in the study without giving a reason, and without it affecting their relationship with their GP or the referring organisation and/or their future treatment and care. The PIS will also provide details of a contact point where participants may obtain further information about the study. Participants will also be informed that although they are under no obligation to provide a reason for withdrawing from the study, it would be helpful information when assessing the study's success.

Following these discussions people who are willing to participate will be asked to complete, sign and date the study consent form, which will also be signed and dated by the person obtaining consent.

Capacity to consent

To be eligible for participation in the REACT study, participants must have the capacity to give their own informed consent. If a member of the research team considers that a participant is incapable of understanding what is expected of him or her as a subject in the study, it is not permissible for informed consent to be obtained from a guardian. The study requires daily responsibilities that cannot be easily assumed by other people. A reassessment of capacity will take place at 12 months.

Storage of consent forms

A copy of the signed Informed Consent form will be given to the participant. The original signed form will be retained in the relevant Site File. A copy of the form will be scanned and stored at the local trial site.

Data Entry of Informed Consent Documents

Pertinent information from the informed consent forms will be entered into the secure REACT database.

7.3 The randomisation scheme

Eligible participants will be randomised to one of the two arms via a secure, centralised web-based randomisation website designed and maintained by the Peninsula Clinical Trials Unit. Randomisation will be performed using a minimisation algorithm to balance groups in terms of study site (Bristol, Birmingham, Exeter), age group, gender and initial functional ability.

During the pilot phase the randomisation will be 2:1 (Intervention/Control) in order to enable testing of the intervention processes as early as possible. The main trial randomisation will be 1:1.To perform randomisation an authorised member of the research team will access the randomisation website using unique username and password log-in details. The website will require entry of patient's initials, date of birth and stratification variables (study site, age group, gender and initial functional ability). The randomisation website will also generate a unique study ID number for the participant when they are randomised. Couples presenting together at the screening where both are eligible and willing to be involved in the study will be randomised together to reduce contamination.

In the event that more than 30 individuals (15 intervention, 15 controls) are recruited within a study site a small waiting list will be maintained. In the event that an individual drops out of the study (intervention or control) during the first 2 weeks they may be replaced by a member of the waiting list although they will still be followed up and included in the ITT population. This will ensure the group nature of the intervention is maintained. As the PenCTU database only allows 30 participants to be randomised to a group, if this situation occurs a second group will be set up on the database where replacement participants will be entered and randomised as normal

If a new group is subsequently started at the site then the waiting list will be randomised into the new group. If the new group does not start within 3 months of the original baseline assessment then a new assessment will be required.

7.3.1 Method of implementing the allocation sequence

Confirmation that randomisation has been performed will be communicated in a blinded fashion to investigator site staff and key members of the central research team. Communication will be achieved via emails automatically generated by the randomisation website.

The CTU will send the study ID numbers of intervention and control participants to a departmental administrator at the University of Bath. The administrator, who will have no involvement in the research elements of the study, will telephone participants to inform them of their allocation and send them a confirmation letter using the contact details collected at the baseline clinic visit.

During the telephone call to the control group, participants will be invited to their first social/education group session which will be held 10-12 weeks after allocation. They will also be mailed a REACT

information pack containing healthy ageing advice. A thank you for participating card will be sent to confirm the date of the social/education group session. Letters to participants in the intervention group will advise participants of the date, venue and transport arrangements for their attendance at REACT sessions. The departmental administrator will follow this up with a telephone call shortly before the day of the first session to re-confirm the arrangements and discuss any practical issues.

7.4 Blinding

Allocation concealment: We will ensure allocation concealment until the point of randomisation which will be after collection of all baseline measures.

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 research team remain blinded to group allocation. At follow-up data collection visits, patients will be asked not to reveal which group they are in. Allocation codes will be locked away by the CI until the database is closed for analysis.

Data will be coded so that those performing the statistical and economic analyses will also be blinded. Given the study design, we do not anticipate a substantial risk of contamination (i.e. exposure of the control participants to the REACT intervention). However, as part of their briefing on entry to the study (and at follow up measurement visits), participants in the intervention arm will be asked not to share or discuss the content of the intervention sessions with any control participants they may be in touch with, for the duration of the study. The possibility of contamination of control patients by intervention deliverers will be minimised by giving clear instructions to the intervention deliverers not to provide intervention materials or information to any participants not assigned to the intervention group. Attrition bias will be minimised by having robust trial procedures to prevent data loss and also analysing the data by intention to treat (ITT).

In order to ensure a balance of intervention and control participants in the fMRI imaging sub-study the University of Oxford team will receive a review of the figures at two points in the recruitment process (showing only the number of recruits from each group). The University of Oxford will consult on additional recruitment strategies to ensure a balanced representation of intervention and control participants in the fMRI scanning sub-study. In the event of a significant imbalance in group sizes, we would adjust the rate of invitation for different groups to redress the imbalance. For example, if it is found that group A are significantly under-represented relative to group B at one of our check points, then the trial administrator would pass on to the Oxford team details for two group B participants who have expressed an interest in participation in the fMRI imaging sub–study for every group A participant passed on.

7.5 Unblinding research

The DMEC will undertake safety data reviews every 12 months after recruitment begins, and all SAEs will be reported to them. The DMEC will be responsible for identifying any need for unblinding. The DMEC will also periodically reviewing unblinded overall safety data to determine patterns and trends of events, or to identify safety issues, which would not be apparent on an individual case basis.

7.6 Baseline data

Data collected at baseline

After written informed consent has been obtained, the PI (or authorised researcher) will confirm eligibility and collect the following information from participants:

Demographics BMI, deprivation index for residence, age, gender, level of education attained, school leaving age, marital status, housing type, ownership/rental status, caring responsibilities and ethnicity.

The Short Physical Performance Battery (SPPB), 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]).

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). Accelerometers will be worn for one week at each measurement point.

Sedentary time and breaks in sedentary time per day assessed by accelerometry.

Self-reported physical activity (PASE questionnaire)[53] .

Hand grip strength of the dominant hand using a digital dynamometer (predictive of functional limitation)[87].

Brief measures of mental well-being the Social Well-Being scale of the Ageing Well Profile[89] (6 items)); Sleep Condition Indicator[88] (8 item) pain (Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) (5 item).

Health-related quality of life (EQ-5D, SF-36).

Activities of daily living (ADL) will be measured with the Mobility assessment tool-short form (MAT-sf (See Appendix 5)), SF36 and EQ-5D.

Medical history, Falls Inventory and Health and Social Service Usage

The UK Biobank Healthy Minds Questionnaire will be used to assess memory, attention and executive function (See Appendix 9). These assessments consist of computerised tasks of reaction time, verbal reasoning, digit recall, trail making, digit-symbol substitution and the paired associates learning test which take 20-25 minutes to complete.

Our colleagues at the FMRIB centre at Oxford University will lead the fMRI imaging 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 acquiring structural and functional brain MRI measures for a sub-sample of participants, modelled on the UK Biobank Imaging extension study. This will take place at the Clinical Research and Imaging Centre, Bristol (CRIC) and will involve a 3T MRI scan lasting approximately 60 minutes, to include whole brain T1-weighted MRI, T2*-weighted MRI, diffusion weighted imaging and resting state functional MRI. Participants taking part in this sub-sample will also complete a more detailed battery of computerised cognitive tests targeted at executive function, attention, memory and processing speed and a gait analysis. The latter uses a gait analysis device to obtain detailed spatio-temporal measures of gait, such as gait speed and gait variability (stride-to-stride fluctuations) enabling examination of the association between mobility and cognition. The assessment will require participants to walk over 10-meters twice and takes about 2-3 minutes.

As part of the REACT process evaluation 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. For full details of the Process Evaluation see Appendix 10.

The person conducting the assessments will be responsible for checking completed questionnaires before participants leave the assessment premises, and will make every effort to ensure missed or spoiled questions are addressed in the interests of maximising data completeness.

Detailed instructions for conducting the SPPB, using a digital dynamometer, issuing accelerometers and conducting the questionnaires will be provided to researchers as part of the Site File. Research staff at all sites will also receive study-specific training in each of these procedures delivered by members of the study team.

Details of the baseline assessment visit will be recorded in the baseline Case Report Form (CRF).

7.7 Trial assessments

The primary outcome (SPPB score) and physical activity will be assessed at baseline, 6, 12 and 24 months. Other secondary outcomes will be assessed at either baseline, 6, 12, and 24 months or baseline, 12 and 24 months. Process evaluation questionnaires assessing mechanisms of change will be conducted at baseline, 6, 12 and 24 months. MRI scans will be administered at baseline, 6 and 12 months.

Table 1 Assessment schedule

Visit type	Scr	Scr	Fu	Fu	Fu
Visit code		SV1	F06	F12	F24
Visit number		1	2	3	4
Telephone call	1				
Activity/assessment Month	-0.5	0	6	12	24
Form Name					
Verbal consent	X				
Telephone screening (some elements of inclusion and exclusion criteria)	X				
Written informed consent		X			
Contact information update	X	X	X	X	X
Demographic, social, economic	X				
SPPB battery		X	X	X	X
Accelerometry		X	X	X	X
Height and weight (weight only at 12 months)		X		X	X
MoCA – Montreal Cognitive Assessment		X	X	X	X
PASE questionnaire (10 item)		X	X	X	X
Dynometer (hand grip strength)		X	X	X	X
Ageing Well profile (6 items social well-being scale only at Bath/Bristol site)		X		X	X
Sleep Condition Indicator		X	X	X	X
Pain (Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC)		X			X

Health-related quality of life (EQ-5D, SF-36)		X	X	X	X
Mobility assessment tool-short form (MAT-sf)		X	X	X	X
Cognitive function (UK Biobank Healthy Minds Questionnaire)		X	X	X	X
Medical history		X	X	X	X
Falls Inventory		X	X	X	X
Health and Social Service Usage		X	X	X	X
Process measures					
Exercise Adherence rating scale		X	X	X	X
Attitudes to and experience of physical activity (pa)		X	X	X	X
Keeping track of physical activity		X	X	X	
Feedback on REACT (Intervention group only)			X	X	
Co-interventions and health changes			X	X	X
Interviews			X	X	X
Focus groups				X	
(fMRI imaging substudy) MRI scan, detailed cognitive assessment and gait analysis		X	X	X	

7.9 Process Evaluation

During the development of the REACT process evaluation plan account was taken of the recommendations outlined in the MRC guidance on process evaluation. A full description of the process evaluation is available in Appendix 10. Section 1 outlines key points from the MRC guidance that have been considered. Section 2 describes a logic model for REACT which provides a basis for the process evaluation. Section 3 provides the hypotheses tested in the process evaluation. Sections 4 and 5 summarise plans for the process evaluation, including both qualitative and quantitative data collection. Section 6 provides the topic guides for the qualitative evaluation and section 7 provides a list of references.

7.10 Data collected via primary care

Post-randomisation GPs will be requested to provide the e-Frailty Index score for participants for comparison with their REACT baseline Short Physical Performance Battery (SPPB) scores. In addition GPs will be asked to provide a summary of the gender and ages of all patients receiving a REACT invitation to establish the representativeness of our study sample.

7.11 End of trial

The South East Coast – Surrey Research Ethics Committee which gave a favourable opinion of the research will be notified of its conclusion, in writing, using the appropriate form within 90 days of the end of the study. A summary of the final research report will be submitted to the REC within 12 months of the end of the study.

A draft final report will be provided to NIHR within 14 days of the project end date following the NIHR guidance: www.journalslibrary.nihr.ac.uk/authors

This report will be sent by NIHR for external peer review and a revised report will be submitted within six weeks.

8 TRIAL INTERVENTION

8. Planned interventions

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 and promote long-term compliance.

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 (See Appendix 1). 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, plus 15-20 minutes 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 (See Appendix 3). 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, in the neighbourhood or at a local physical activity session. 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 while continuing with a weekly centre-based physical activity session followed by a short social session. Participants will enact action plans that were made during the transition phase and will be supported through group social/education meetings once a month. At this stage we may 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 taster activity sessions (supplied by our collaborators and partners, other local service providers /companies, including health walks, 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.

Control Arm: After completion of baseline assessments, participants allocated to the control group will be given information regarding events and activities in their local community. They 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 the completion of the six month assessment, control participants will be invited to a further 60-minute group social/education session. Between the 12 and 24-month data collection sessions, controls will be invited to a further 60-minute group session (See Appendix 2 for details). After 24-month data collection, controls 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.

Assessment of intervention fidelity and participant adherence

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.

9 SAFETY REPORTING

9.1 Recording and reporting of SAEs

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 Birmingham standard operating procedure for reporting research related Adverse Events (AEs) will be adopted.

9.2 Definitions

Adverse Event (AE) is any untoward medical occurrence, elective hospitalisation/surgery, unintended disease or injury or any untoward clinical signs in subjects, users or other persons **whether or not related to any research procedures or to the intervention.**

Non-serious adverse events which are not related to study procedures or to the intervention will **not** be reported in this study.

The expression 'reasonable causal relationship' means to convey, in general, that there is evidence or argument to suggest a causal relationship. PIs or Research Assistants will assess the causal relationship between reported events and trial participation according to the standardised guidance given below:

Table 2 Causal relationship between reported events and trial participation	
Relationship	**Description**
Unrelated	There is no evidence of any causal relationship
Unlikely	There is little evidence to suggest there is a causal relationship (e.g. The event did not occur within a reasonable time after the study period). There is another reasonable explanation for the event (e.g. The participant's clinical condition, other concomitant treatment).
Possible	There is some evidence to suggest a causal relationship (e.g. Because the event occurs within a reasonable time after the study period) However, the influence of other factors may have contributed to the event (e.g. The participant's clinical condition, other concomitant treatments).
Probably	There is evidence to suggest a causal relationship and the influence of other factors is unlikely.
Definitely	There is clear evidence to suggest a causal relationship and other possible contributing factors can be ruled out.

Seriousness

Any adverse event or adverse reaction will be regarded as serious if it:

i. results in death;

ii. is life threatening;

iii. requires non-elective hospitalisation, prolongation of existing hospitalisation or elective hospitalisation that may be related to taking part in the study;

iv. results in persistent or significant disability or incapacity

If the description of the event leading to an elective hospital admission suggests in any way that the cause might be related to taking part in REACT, this will be investigated using the normal SAE pathway. Therefore, an adverse event meeting any one of these criteria will be a **Serious Adverse Event (SAE).** In this study, all serious events will be reported regardless of relatedness. Any non-serious adverse events (regardless of relatedness) will not be reported. All reportable events will be followed until resolution where possible or until the end of the data collection period.

Reportable events

Table 3 - Reportable adverse events			
Event type	Reported by	Reported to	Timeframe
Serious Adverse Event (SAE)	Local PI, TM or RA	CI, DMEC, Sponsor	Within 24 hours*

- *To the of the DMEC by PI (or authorised delegate)*

Non-serious AEs will not be recorded, regardless of relatedness. The DMEC will maintain a register of all reported serious adverse events.

All **SAEs** occurring from the time of **written informed consent until** 30 days post cessation of trial sessions will be recorded on the University of Birmingham report of serious adverse event form (See Appendix 11) and sent to the chair of the DMEC **within 24 hours** of the research staff becoming aware of the event. Once

all resulting queries have been resolved, the original form will be posted to the chair of the DMEC and a copy be retained on site.

For each **SAEs** the following information will be collected:

- full case description
- event duration (start and end dates, if applicable)
- action taken
- outcome
- seriousness criteria
- causality (i.e. relatedness to trial), in the opinion of the investigator
- whether the event would be considered expected or unexpected.

Any change of condition or other follow-up information will be sent to the chair of the DMEC as soon as it is available or at least within 24 hours of the information becoming available. Events will be followed up until the event has resolved or a final outcome has been reached.

9.3 Reporting related and unexpected SAEs

Adverse events will be collected at the research measurement events and the physical activity sessions via patient reporting. In addition if a participant does not attend two consecutive physical activity sessions or one measurement session, they will be contacted by telephone and if the reason for non-attendance is an adverse event this will be recorded. The PI/RA will question patients about adverse events and will be responsible for judging any relationship to the study procedures. The PI/RA will then complete the NRES report of serious adverse event form using information from the SAE form and send it to the CI for review.

The PI and CI will review the form and when happy with the content the CI will sign the form.

The CI will send the following to chair of the DMEC who will decide if the ethics committee who gave favourable opinion and the Sponsor (PVC, Research) need to be informed.

(i) A cover letter including the REC number.

(ii) The NRES report of serious adverse event form

(iii) A copy of the SAE form.

(d) The RA will file a copy of the form and cover letter in the site file. If there is no missing data and the event has been resolved file the SAE form will also be filed in the site file.

Adverse events that are serious, as reported by the patient, will be documented in the purpose-designed CRF. Multiple symptoms that are serious will be recorded as separate events.

Processing serious adverse event forms

On receipt of a completed SAE form, the chair of the DMEC will assign a unique SAE number and confirm receipt of the event to the reporting site. If complete information is unavailable at the time of reporting, all appropriate information relating to the SAE will be forwarded to the DMEC as soon as possible.

Summary reports listing all reportable adverse events will be compiled by the DMEC and sent to the CI, Sponsor and the TSC on a quarterly basis (or more frequently if the DMEC considers this to be necessary).

9.4 Responsibilities

The Chief Investigator is responsible for:

Reporting details of all SAEs to the DMEC using the study specific SAE Form within 24 hours of becoming aware of the event.

Providing the follow up report (if required) to the DMEC.

Providing any further information that has been requested to the DMEC.

In conjunction with the TSC medical advisor reviewing the SAEs for seriousness, causality and expectedness; classifying the SAE (related).

Reviewing and signing the NRES "Report of SAE Form".

Sending the reports to the DMEC within the specified guidelines.

The Principal Investigators are responsible for:

Review the SAE form with the CI.

Completing (with the RA) the SAE form

The Trial Management Group/Trial Steering Group are responsible for:

Discussing all SAEs that have been received.

When required: giving consensus to a SAE classification (consensus reached when at least 2-3 members replied and agreed).

TSC will periodically review safety data and liaise with the DMEC regarding safety issues.

Data Monitoring and Ethics Committee are responsible for:

Discussing all SAEs that have been received.

When required: giving consensus to a SAE classification (consensus reached when at least 2-3 members replied and agreed.)

Providing summary reports listing all reportable adverse events to the CI, Sponsor and the TSG on a quarterly basis (or more frequently if the DMEC considers it to be necessary).

Deciding which SAEs need to be reported to the REC

The DMEC will periodically reviewing unblinded overall safety data to determine patterns and trends of events, or to identify safety issues, which would not be apparent on an individual case basis.

The Research Assistants are responsible for:

Following up any reported SAEs.

Contacting any participants who do not attend a measurement session or two consecutive physical activity sessions to discover if this is due to an SAE.

Scanning/typing and verifying the SAE on to the Study database and chasing missing information.

Filing all documentation in the site file.

Sponsor

Reporting safety information to the CI for the ongoing assessment of the risk / benefit.

Reporting safety information to the independent oversight committees (Data Monitoring and Ethics Committee (DMEC) and Trial Steering Committee (TSC)).

Checking for (annually) and notifying PIs of updates to the Reference Safety Information for the trial annually.

9.5 Notification of deaths

All deaths, including deaths deemed unrelated to the trial, if they occur earlier than expected will be reported to the DMEC immediately.

9.6 The type and duration of the follow-up of subjects after adverse events.

Following up SAEs (where data missing or event not resolved)

(a) Where there is missing data/queries or the event is not yet confirmed as resolved, the RA will manage the event/chase the data until the form is complete.
(b) RA will update the database with all new information received.
(c) When the SAE form is complete the RA will file the SAE form in the site file.

9.7 Development safety update reports

The CI will provide DSURs once a year throughout the trial, or on request, to the Ethics Committee and Sponsor.

10 STATISTICS AND DATA ANALYSIS

10.1 Sample size calculation

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 in Section 3.3., 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. In the LIFE study, the standard deviation for the change in SPPB scores from baseline to 2 years was 2.2 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.

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. A 2:1 randomisation process was applied in the internal pilot phase. A 1:1 randomisation process without rebalancing will be applied in the main trial resulting in an allocation ration of 1.11:1. On the assumption that the effect size, the dropout rate and the significance level we are interested in remains unchanged then our power will reduce to 84.9% (from 85% power using two sided 5% significance if the sample was rebalanced).

10.2 Planned recruitment rate

For details of the planned recruitment rate see Section 7.1.1 (Recruitment response rates)

10.3 Statistical analysis plan

10.3.1 Summary of baseline data and flow of patients

For details of data collected at baseline see Section 7.6 (Baseline data). The flow of participants through the study is illustrated by the Participant Flow Chart on Page 13.

10.3.2 Primary outcome 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.

10.3.3 Secondary outcome analysis

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.

10.4 Subgroup analyses

We will compare those with high adherence (75% attendance) and those with lower adherence and comparing participants with one or less known medical conditions to those with more (multiple comorbidity), response to exercise based on SPPB score.

10.5 Adjusted analysis

Using appropriate descriptive statistics, we will assess any imbalance between the trial arms at baseline and describe the characteristics of participants. As participants are randomised using the method of minimisation we are not expecting significant imbalance between groups. However, the minimisation variables (age, gender, SPPB) will be adjusted for in the statistical analysis.

10.6 Criteria for the premature termination of the trial

A full data analysis protocol including stopping criteria 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.

10.7 Subject population

REACT participants will be sedentary, community living, older persons aged 65 and over, with functional limitations (i.e. who are at risk of major mobility limitations), but who are still ambulatory, i.e. can still walk. Bristol/Bath, Birmingham and Devon will be target areas for recruitment that represent a broad range of socio-economic status.

As a pragmatic trial of intervention effectiveness rather than efficacy, the primary ITT analysis makes no attempt to take account of actual intervention received and will include all data on all participants.

The per-protocol analysis will seek to establish the efficacy of the treatment 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. We will also conduct analyses to examine the representativeness of the sample recruited in comparison to a) the populations of the areas where we recruited and b) the population of people invited (by letter) into the study. In addition, using logistic regression analyses, we will also examine the sensitivity and specificity of the eFrailty index for identifying people with moderate frailty as indicated by a SPPB score of 4-9 (as well as other possible SPPB cut-offs).

10.8 Procedure(s) to account for missing or spurious data

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.

10.9 Other statistical considerations.

The Statistical analysis plan (SAP) will be specified as part of the publication of the trial protocol. Hence any changes to the SAP will be noted as amendments to the original protocol such that both the original intention the changes and the purpose of the changes will be clear. All changes will be approved by the Trial Steering Committee.

10.11 Economic evaluation

The economic evaluation will establish the resources for estimating the cost of REACT. It will also estimate the incremental cost-effectiveness of the REACT intervention compared to control i.e. incremental cost per unit of health outcome (primary outcome, Quality-Adjusted Life Year (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 and analyses will cover the three phases of the intervention (adoption, transition and maintenance), and will include set-up and training costs associated with introduction and implementation. The pilot phase of the proposed research will be used to finalise methods for reporting intervention-related resource use, e.g. using sampling methods and self-reported data. Methods for estimating resource use and cost for REACT will include within-trial data reporting, via trial researchers and via those delivering the intervention and will be collected at baseline, 6, 12 and 24-month. Unit costs will be obtained from available sources. 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). Incremental costs will be combined with data on effectiveness and health outcomes, to present a policy relevant cost-effectiveness analyses (CEA), appropriate for a range of policy makers. 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). 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.

11 DATA HANDLING

11.1 Data collection tools and source document identification

Study Numbering

Each participant will be allocated a unique study number on consenting to the study and will be identified in all study-related documentation by their trial number and their acrostic, including the first 3 letters of their surname and the first two letters of their first name.

Data Collection

Data will be recorded on study specific data collection forms, the Case Report Forms (CRFs), by the research team at each site. All persons authorised to collect and record trial data at each site will be listed on the trial site delegation logs, signed by the relevant PI. Source data will include all data recorded straight into the CRF, SPPB results, accelerometer data and grip strength data. Audio files and transcriptions of the data will be collected by the Process Evaluation Team, comprising REACT PhD student, PIs and RAs.

11.2 Data handling and record keeping

Data handling

Completed CRFs will be checked and signed at the assessment sites by a member of the research team before being taken to the local research site. Data from the original CRF pages and SPPB result forms will be entered on to a password-protected website designed and maintained by the Peninsula Clinical Trials Unit. All CRF pages and data collection forms will be tracked using the website. Double-entered data will be compared for discrepancies using a report available on the website. Discrepant data will be verified using the original paper data sheets and incorrect values will be updated. Audit trails will be used to record all change to study data. Accelerometer data and data from the computerised UK Biobank Healthy Minds Questionnaire will be imported directly into the study database at each site. Anonymised brain imaging data and data from detailed cognitive assessments for the fMRI imaging sub-study will be stored on password protected secure servers at the Universities of Bristol and Oxford.

Data Confidentiality

Participant names and addresses will be collected for the purpose of managing questionnaires, intervention delivery and process evaluation interviews. Investigators will ensure that the participants' anonymity is maintained on all other documents. Within each trial site, anonymised and identifiable study data will be stored separately, to prevent the identification of participants from research records, in locked filing cabinets within a locked office. Electronic records will be stored at each site in a SQL server database, housed on a restricted access, secure server. Data in the database will be backed up daily by IT services at the Universities of Bath, Birmingham and Exeter. Back-ups will be accessible for up to 6 months. The website will be encrypted using SSL. Anonymised brain imaging data and data from detailed cognitive assessments for the fMRI imaging sub-study will be stored on password protected secure servers at the Universities of Bristol and Oxford. Data will be collected and stored in accordance with the Data Protection Act 1998. Direct access to the trial data will be restricted to members of the research team, with access granted to the Sponsor on request. Access to the database will be overseen by the CI and trial coordinator. Copies of original study data retained at trial sites will be securely stored for the duration of the study prior to archiving. Audio recordings and participant names and addresses will be stored on a restricted access, secure servers at the Universities of Bath, Birmingham and Exeter.

All data entered into the website provided by the Peninsula Clinical Trials Unit will be stored in a SQL Server database, housed on a restricted access, secure server managed by Plymouth University. Data in the database will be backed up daily by IT services at Plymouth University. Back-ups will be available for the entire duration of the study. All data transferred to and from the website to the SQL Server database will be encrypted using SSL. Data will be collected and stored in accordance with the Data Protection Act 1998. Direct access to the trial data will be restricted to members of the research team, with access granted to the Sponsor on request. Access to the website will be overseen by the CI and trial coordinator.

11.3 Access to Data

Direct access will be granted to authorised representatives from the Sponsor, host institutions and the regulatory authorities to permit trial-related monitoring, audits and inspections.

11.4 Archiving

Following completion of trial data analysis, the Sponsor will be responsible for archiving the study data and essential documentation in a secure location. No trial-related records will be destroyed unless or until the Sponsor gives authorisation to do so. The NIHR's Policy on Open Access will be adhered to and data supporting published findings will be made accessible.

12 DATA MONITORING, AUDIT & INSPECTION

The PI or RA will check completed case report forms for missing data or obvious errors before the forms are sent for data entry. Data will be monitored for quality and completeness by each site and every effort will be made to recover data from incomplete forms where possible. The PIs will oversee data tracking and data entry and initiate processes to resolve data queries where necessary. The Trial manager will devise a monitoring plan specific to the study which will include both data monitoring strategies and trial site visits as appropriate.

Participating sites will be required to permit a representative of the TSC or representative of the sponsor, to undertake study-related monitoring to ensure compliance with the approved study protocol and applicable SOPs, providing direct access to source data and documents as requested.
All study procedures will be conducted in compliance with the protocol and according to the principles of the International Conference on Harmonisation Good Clinical Practice (ICH GCP). Procedures specifically conducted by the CTU team (e.g. randomisation) will be conducted in compliance with CTU standard operating procedures (SOPs).

13 ETHICAL AND REGULATORY CONSIDERATIONS

13.1 Research Ethics Committee (REC) review & reports

The study 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 study will be conducted in accordance with the Research Governance Framework for Health and Social Care, Second edition (2005). The study will be supported by the UKCRC-registered PenCTU (Registration Number 31), sponsored by the University of Birmingham and approved by a recognised NHS REC and the HRA. The study will be adopted by the NIHR Clinical Research Network (CRN).

The trial will be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki, and that are consistent with GCP. Any amendments to the protocol will be submitted for REC approval as appropriate.

On request, the Chief/Principal Investigators will make available relevant trial-related documents for monitoring and audit by the Sponsor, the TSC and the relevant Research Ethics Committee.
Annual progress reports will also be submitted to the REC using the recognised National Research Ethics Service (NRES) template. An end-of-trial declaration will be provided to the REC within 90 days of trial conclusion or within 15 days of trial termination in the event the trial is prematurely terminated.

The Sponsor will draw up an agreement with the PenCTU regarding study responsibilities, which will be agreed and signed by the authorised representatives of each party.

Substantial amendments that require review by REC will not be implemented until the REC grants a favourable opinion for the study.

All correspondence with the REC will be retained in the Trial Site File.

An annual progress report (APR) will be submitted to the REC within 30 days of the anniversary date on which the favourable opinion was given, and annually until the trial is declared ended

The Chief Investigator will produce the annual reports as required.

The Chief Investigator will notify the REC of the end of the study.

If the study is ended prematurely, the Chief Investigator will notify the REC, including the reasons for the premature termination

Within one year after the end of the study, the Chief Investigator will submit a final report with the results, including any publications/abstracts, to the REC.

13.2 Peer review

The REACT draft trial protocol was reviewed by the TMG, the TSC and the DMEC prior to submission. Their comments were incorporated into the final version of the protocol, which was also reviewed by two US colleagues who were integral to the LIFE trial on which REACT is based. The REACT grant application was given favourable review by the NIHR panel.

13.3 Public and Patient Involvement

Our preparatory work has involved extensive service user involvement [99]. We established an advisory group of older people participating in local community initiatives as part of our AVONet project [48]. They participated in focus groups and decision-making workshops, in which they identified criteria for selecting community-based activity interventions for promoting active ageing. They systematically ranked different intervention models based on their likely cost-effectiveness, feasibility, attention to maintenance issues, and potential to meet older people's needs. This identified three 'best bet' interventions. The first choice was a structured, community and group-based activity programme with systematic support for transition to home-based exercise. Further PPI work identified the LIFE intervention as the best evidence-based example of such an approach. Hence, our intervention selection is solidly grounded in service users' and providers' perspectives.

The Trial Management Group has three service user representative members and the Trial Steering Committee has one user representative member who will be involved in overseeing and guiding all aspects of the study. In addition, Advisory Groups, consisting wholly of service user representatives, will be established at each trial site to review study processes and materials.

REACT participants will play a central role in the dissemination of study findings; reviewing papers and presentations and attending events.

13.4 Regulatory Compliance

For the fMRI imaging sub-study we will implement a standard operating procedure for dealing with incidental findings (detection of previously unknown pathology on a brain scan). This procedure will follow the following pipeline:

a) Researcher spots a potential incidental finding and passes it on to a radiographer - for reasons of patient confidentiality this is the end of the researcher's involvement (this step may be bypassed in the radiographer spots the incidental finding during data acquisition).
b) If radiographer deems it benign no further action is taken, otherwise s/he refers on to a suitable clinician (neurologist, neuroradiologist).

If a clinician deems it necessary to follow up with patient, s/he will inform the participant's GP of an incidental finding. In this way, if deemed necessary by the study's neuroradiologist, the participant will be informed of the finding by their own doctor, a health professional they are already familiar with and who is familiar with their medical history.

If a participant requests that their scan(s) be released to their GP they will be asked to sign an additional consent form specifically giving permission for this to be done. A neurologist's report will accompany the MRI scans.

13.5 Protocol compliance

Prospective, planned deviations or waivers to the protocol will not be allowed, e.g. subjects who do not meet the eligibility criteria or restrictions specified in the trial protocol will not be enrolled.

Any accidental protocol deviations will be adequately documented on the relevant forms and reported to the Chief Investigator immediately.

Deviations from the protocol which occur frequently will be addressed immediately and if appropriate will be classified as a serious breach.

13.6 Notification of Serious Breaches to GCP and/or the protocol

A "serious breach" is a breach which is likely to effect to a significant degree –

(a) the safety or physical or mental integrity of the subjects of the trial; or
(b) the scientific value of the trial

The Sponsor will be notified immediately of any case where the above definition applies during the trial conduct phase. Guidance for reporting potential serious breaches of good clinical practice / trial protocol in clinical research sponsored by the University of Birmingham will be adhered to (See Appendix 12).

13.7 Data protection and patient confidentiality

Participant names and addresses will be collected for the purpose of managing questionnaires, intervention delivery and process evaluation interviews. Investigators will ensure that the participants' anonymity is maintained on all other documents. Within each trial site, anonymised and identifiable study data will be stored separately, to prevent the identification of participants from research records, in locked filing cabinets within a locked office. Electronic records will be stored at each site in a SQL server database, housed on a restricted access, secure server. Data in the database will be backed up daily by IT services at the Universities of Bath, Birmingham and Exeter. Back-ups will be accessible for up to 6 months. The website will be encrypted using SSL. Anonymised brain imaging data and data from detailed cognitive assessments for the fMRI imaging sub-study will be stored on password protected secure servers at the Universities of Bristol and Oxford. Data will be collected and stored in accordance with the Data Protection Act 1998. Direct access to the trial data will be restricted to members of the research team, with access granted to the Sponsor on request. Access to the database will be overseen by the CI and trial coordinator. Copies of original study data retained at trial sites will be securely stored for the duration of the study prior to archiving. Audio recordings and participant names and addresses will be stored on a restricted access, secure servers at the Universities of Bath, Birmingham and Exeter.

All data entered into the website provided by the Peninsula Clinical Trials Unit will be stored in a SQL Server database, housed on a restricted access, secure server managed by Plymouth niversity. Data in the database will be backed up daily by IT services at Plymouth University. Back-ups will be available for the entire duration of the study. All data transferred to and from the website to the SQL Server database will be encrypted using SSL. Data will be collected and stored in accordance with the Data Protection Act 1998. Direct access to the trial data will be restricted to members of the research team, with access granted to the Sponsor on request. Access to the website will be overseen by the CI and trial coordinator.

Access to data

Access to the data will be strictly limited to members of the research team; however participating sites will permit a representative of the CTU or representative of the sponsor, to undertake study-related monitoring to ensure compliance with the approved study protocol and applicable SOPs, providing direct access to source data and documents as requested.

Archiving

Following completion of trial data analysis, the Sponsor will be responsible for archiving the study data and essential documentation in a secure location. No trial-related records will be destroyed unless or until the Sponsor gives authorisation to do so. The NIHR's Policy on Open Access will be adhered to and data supporting published findings will be made accessible.

13.8 Financial and other competing interests for the chief investigator, PIs at each site and committee members for the overall trial management

The Chief Investigator, site PIs and TMG members have no competing interests that might influence trial design, conduct, or reporting. Any that occur during the period of the trial will be noted to the TMG meetings and minuted. All co-applicants will sign a competing interest form at the beginning of the trial and at the end of the trial unless there is a need for an updated form during the trial.

13.9 Indemnity

The University of Birmingham has arranged Public Liability insurance to cover the legal liability of the University as Research Sponsor in the eventuality of harm to a research participant arising from management of the research by the University.

The University of Birmingham holds Professional Indemnity insurance to cover the legal liability of the University as Research Sponsor and/or as the employer of staff engaged in the research, for harm to participants arising from the design of the research, where the research protocol was designed by the University.

The University of Birmingham's insurance policies do not provide an indemnity to collaborators. As Research Sponsor we will ensure as far as reasonably practicable at the outset of the study that collaborators hold appropriate legal liability insurance.

The University of Birmingham has not made arrangements for payment of compensation in the event of harm to the research participants where no legal liability arises.

Evidence of insurance cover is available to download at intranet.birmingham.ac.uk/finance/insurance

13.10 Amendments

Any amendments to the protocol will be submitted for REC approval as appropriate. Substantial amendments that require review by REC will not be implemented until the REC grants a favourable opinion for the study.

13.12 Access to the final trial dataset

Prior to the first report/publication being made (the publication(s) reporting the results of the research as a whole), the collaborators cannot report on the results (those collected at their site and from the project as a whole) without first gaining consent from the CI. Thereafter the collaborators can independently publish the results subject to provisions of confidentiality.

The NIHR's Policy on Open Access will be adhered to and data supporting published findings will be made accessible.

Subject to data protection provision (data to be anonymised), the Secretary of State for Health has the right to have access and use data collected and used for the purpose of the project.

14 DISSEMINATION POLICY

14.1 Dissemination policy

Research findings will be disseminated using several channels to ensure maximum exposure:

1. Our OPAL and AVONet websites will be updated to include a section for publishing REACT news and progress. All research presentations and reports will be uploaded and made available for public comments;

2. A one day launch event will be co-hosted with the partner organisations.

3. Showcase events will be delivered at all three sites after completion of REACT to present the findings and celebrate successful lifestyle change stories;

4. At least 5 papers will be submitted for publication in peer reviewed journals, including open access journals (e.g., International Journal of Behaviour Nutrition & Physical Activity), subject-specific journals (e.g., Journal of the American Geriatrics Society) and medical journals (e.g., Annals of Behavioural Medicine, NIHR PHR Journal);

5. Presentations will be delivered at University-sponsored Public Lecture series, national (UK Society of Behavioural Medicine) and International (World Congress of Aging and Physical Activity) conferences, and events organised by local partner organisations;

6. Newsletters will be distributed to participants at the end of each project year and through academic and non-academic partners and the European Network for Action on Ageing and Physical Activity;

7. Social media (including Universities' Twitter accounts and Facebook pages) and local media (newspapers, magazines) will be used to publish news briefings prepared by the Universities' press offices;

8. We will capitalise on the extensive distribution channels of AGE UK to disseminate information in a more visual and user friendly way, and via the Action Age Alliance which involves over 570 partner organisations including eight Government Departments and representatives from public, private and voluntary sectors. Our MRC funded work has already been disseminated via Action Age Alliance (http://ageactionalliance.org/wordpress/wp-ontent/uploads/2014/03/AVONetreport-2014-March.pdf) and we will continue this successful collaboration.

14.2 Authorship eligibility guidelines and any intended use of professional writers

The International Committee of Medical Journal Editors' authorship criteria (detailed below) will be used as the basis for granting authorship of the REACT final trial report.

- Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; AND
- Drafting the work or revising it critically for important intellectual content; AND
- Final approval of the version to be published; AND
- Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

A detailed publication plan with proposed authorship will be developed and agreed by the TMG during the first year of the Trial.
Professional writers will not be used in the development of the REACT trial reports

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16. APPENDICES

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Appendix 1 REACT Ambassador Programme outline

REACT Ambassador Programme
(available to Intervention group members)

Description	The Ambassador Programme is a voluntary training programme and subsequent support system that enables participants in the REACT intervention group to take on roles in the programme that carry responsibility
Objectives	The purposes of the Ambassador Programme are a) to offer a role that provides a higher level of experience to REACT intervention group members, and b) build REACT programme sustainability and sense of local ownership through assistance with recruitment, administration, evaluation and community support
Administration	The Ambassador programme will be administered and delivered by an experienced member of the research team in the first instance. Responsibility will be gradually handed to the local partner organisation who will first attend the training programme and who will receive initial support from the research team.
Roles	A choice of roles will be available: 1. ***REACT Outreach*** for assistance with recruitment and linking REACT with activities in the community 2. ***REACT Support*** for assistance with record keeping, data collection, support of the social/education programme and assisting individual participants
Timing	**Weeks 28-30** Delivery of Ambassador training information and invitations to enrol **Weeks 31-33** 120 minutes x 2 training sessions per week (4 hours total) **Weeks 33-34** Assignment to roles **Week 42** Ambassador sharing event and award of 8 week Certificates **Weeks 35-52** Bi weekly support/mentoring through phone exchange or face to face with the professional in charge of the aspect of work they choose.
Training Session content	**Week 1:** Introduction to the range of Ambassador roles and associated competencies attended by all volunteers who will then chose their role and attend either Week 2 or 3 **Week 2**: Becoming a REACT Outreach Ambassador (how to recruit, publicity, connecting with existing community activities, starting off groups) **Week 3:** Becoming a REACT Support Ambassador (how to support REACT participants, how contribute to social/educational programme, evaluation programme and administration.
Continuing support	1. Bi weekly phone call if off site or face to face if attending the centre combined with follow-up where needed 2. Event organised to bring Ambassadors together and share experiences 3. Award of Ambassador certificates on completion of training and 8 weeks of service

Appendix 2 Intervention group social and educational sessions

REACT Social and educational session programme (Intervention group)

Objectives	REACT social and educational sessions will use evidence-based, person-centred behaviour change strategies to build understanding, intrinsic motivation and self-efficacy for physical activity. At the same time, they are designed to maximise enjoyment, social interaction, a positive, cohesive and collaborative group identity. These aims will support engagement in and maintenance of the physical activity /exercise components of the programme, promote attendance (avoid dropout from) the programme, and motivate people to join the Ambassadors programme to enhance the programme's sustainability. A key focus will be exploring and planning transition of the physical activity /exercise components of the programme to more lifestyle- and community-based activities. The 12 month programme should be presented as a way to "kick start" participants' personal physical fitness and give them the skills and motivation they need to stay fit and active throughout this phase of their lives (retirement /older age). Participants should be encouraged to see the programme as a stepping stone to ongoing health, rather than a time-limited programme of activity that lasts 12 months
Mechanisms of Change	The REACT social /education programme will be largely informal and aimed at maximising social interaction and enjoyment. However, it will contain some structured elements designed to teach participants skills that will help them to plan, implement and maintain a healthy level of physical activity, as well as the muscle-strengthening /function-sustaining exercises that they learn in the exercise sessions. The REACT social programme draws on the following, overlapping (and mutually compatible) theoretical perspectives. Social Cognitive Theory and Self Determination Theory provide the main principles and processes for supporting behaviour change. The Skills for Maintenance (SkiM) model (below) has been used to identify additional processes and techniques to promote maintenance of physical activity /exercise. *Social Cognitive Theory*(Bandura 1986, Bandura 2005) People can learn by observing others and the consequences of their actions, as well as by getting feedback on their own actions. Learners can acquire new behaviours and knowledge by observing and copying a model (another person), especially if they identify positively with the model.. People set goals for themselves based on outcome expectancies (expectation of benefit) and self-efficacy (perceived ability to achieve the behaviour) and direct their behaviour accordingly. They are then motivated to continue a new activity to the

	extent that they get positive feedback about a) benefits and dis-benefits of doing the activity (outcomes) and b) their experienced ability to master /achieve the new behaviour (self-efficacy). The process of behaviour change /maintenance is cyclic, with positive outcomes and the building of self-efficacy, as well as environmental factors acting to reinforce continuation. This process of self-regulation or "learning from experience" requires time for learning of new behaviours to be embedded. *Self-Determination Theory(Deci and Ryan 1985, Deci and Ryan 2012, Fortier, Duda et al. 2012)* Three psychological needs motivate people to initiate and sustain behaviour. These needs are universal and innate and include the need for competence (feeling capable and confident),autonomy (feeling in control of decisions /goals, having motivation that is intrinsic (self-generated)), and relatedness (social engagement, social acceptance /approval of the behaviour, giving support to others). Fulfilling these needs through lifestyle change may lead to an improvement in the social and control /competence domains of the self-concept.(Harter 1999) *The Skills for Maintenance (SkiM) model*(Poltawski, Greaves et al. 2015) This new model focuses on the skills that people need to maintain lifestyle changes. The main premise is that changing your lifestyle can induce psychological and social tensions in your life. The sources of tension for physical activity may include conflict with other priorities, the needs of others, discomfort /lack of enjoyment associated with the new activity, conflict with established habits, or conflict with established beliefs /self-concept (habits of thinking). This tension can be managed in the short term through willpower, self-regulation and regular re-motivation, as well as by making plans to manage any slips and lapses that occur. However, to achieve long-term change requires individuals to either pre-empt and prevent the tension (make changes you can live with /will enjoy), or to resolve it by finding other ways to address the sources of the tension (e.g. to negotiate to resolve conflicts with the needs of others; actively challenge and change unhelpful thoughts and beliefs). Learning from experience and eventual change in self-concept (especially the physical and control /competence self-concept domains in this case) are hypothesised to be important determinants of long-term success. The power of relatedness (from self-determination theory) is acknowledged, but the need to ensure that change is embedded in social support within day-to-day life and not dependent on temporary relationships formed in intervention group settings is an important consideration. It is proposed that the processes of planning, self-regulation, making psychological changes and social interactions to address sources of tension and achieve long-term lifestyle change are teachable skills and techniques have been developed to facilitate this. The model provides a way of ensuring a clear focus on the challenge of long-term maintenance and will be used to the extent that it adds to or extends the above theories. Specifically, this includes the use of techniques to promote habit formation, to plan for sustainability (of social support relationships as well as behaviours), to address hedonistic needs, to address priority conflicts and to

	recognise and reinforce benefits in terms of self-concept change (particularly in the physical, social and competence domains).
Key Competencies	The physical activity session leaders, who will deliver the Social and Educational programme, will be trained in, the intended processes of behaviour change (based on the theoretical principles above) and the delivery of the specific techniques and activities designed to facilitate the intended processes of change (see Content sections below). This will enable the facilitators to identify and reinforce positive steps towards long term physical activity /exercise and to identify and problem-solve any barriers that arise for individual participants. The facilitators will also be trained in person-centred counselling skills (an empathy-building /autonomy-promoting communication style based on motivational interviewing(Miller and Rollnick 2002, Rollnick, Miller et al. 2008)) and group facilitation skills, including: Active listening (“Attending”) and empathic communication Asking open-ended questions Paraphrasing Giving and receiving feedback Managing emotions Summarizing Problem-solving and decision making Group leadership skills Creating social and team cohesion Establishing an enjoyable and rewarding climate Dealing with the difficult/challenging participants
Sessions	
Social only	**Weeks 1-9** 15-20 mins x 2 per week (following each activity session) **Weeks 10-12** 15-20 mins x 1 per week (following one activity session) **Weeks 13-25** No social only session – replaced by Social/Education session **Weeks 26-52** 15-20 mins x 1 per week (following each activity session)

Content	Processes of change
During week 1-12 these short social sessions will focus on building social connectedness, group identity and cohesion. As the Ambassadors programme develops, veterans of the programme may have input to these sessions. Weeks 1-3 will incorporate	Social connectedness, group identity and cohesion. Relatedness (internal and external to the programme)

	Ice breaking activities and team activities to facilitate 'getting to know each other' An overview of the programme /what is to come – presenting the programme as a "kick start" or stepping stone to ongoing health, rather than a time-limited activity. . Weeks 4-12 will include One or more "Why are we here? /What are we doing?" session will discuss the benefits of exercise and physical activity (especially walking) and develop a clear understanding about what types of activity and exercise are needed to support healthy aging (e.g. maintaining independence, reducing the risk of cardiovascular problems). The aim is to build a clear understanding of the rationale for the programme (preventing the spiral of decline that can happen in older age whereby ageing leads to a lack of activity, which leads to muscle-wasting (including muscles needed for balance and general mobility) which leads to a further lack of activity) Reflections on the Activity Session - successes, benefits and challenges (every other session will include this activity) Getting motivated: A facilitated discussion to help people build a positive image of themselves in the future and to build intrinsic motivation to stay with the programme and to engage in and sustain physical activity and mobility-promoting exercise. Problem-solving and breaking down barriers (especially concerns about enjoyment of activities /pain or discomfort, difficulty of exercises, engaging external support for attendance) Input/suggestions on the session delivery/content within the constraints of the REACT model Light hearted and fun physical games Refreshments (tea and coffee) will be served at all sessions.	Competence /self-efficacy Group identity and cohesion Building outcome expectancies /perceived benefits Addressing hedonistic needs
Social and Education	**Weeks 9-25** 45 min x 1 per week (following activity session)	
	Content	Processes of change

	These sessions will consist of a series of (17) classes, workshops, trial sessions and field trips/outings aimed at reinforcing awareness of the benefits of physical activity and muscle-strengthening /function-sustaining exercises relevant to older adults, supporting the mechanisms of change outlined above and exploring/trialling community-based activities, as well as supporting planning and implementation of the transition towards building the exercise components of the programme into participants' day-to-day lives and making sure that they also get the recommended 150 minutes per week of moderate intensity physical activity. Enjoyment and building of intrinsic motivation will be central throughout. Workshop topics will include: 1) Physical Activity and Exercises for Successful Ageing. The "Why are we here? /What are we doing?" session at the start of the programme will be revisited to discuss the benefits of exercise and physical activity (especially walking) and develop a clear understanding about what types of activity and exercise are needed to support healthy aging 2) Staying motivated: Person-centred facilitation to help people further build and reinforce an understanding of their own reasons for wanting to maintain physical activity /exercise (ideally based on their experiences of benefit as they progress though the programme). Discussion should help people build a positive image of themselves in the future and intrinsic motivation to stay with the programme. 3) A discussion of the role of lighter activity to reduce and break up the amount of time being sedentary. 4) A menu of community based /day-to-day physical activity options will be developed by each local provider (this may include some of their existing services) to help people choose what activities to try. 5) Goal setting for sustainable transition of PA into everyday life. . 6) Self-monitoring – are you getting enough? • Self-monitoring of physical activity and of fitness /intensity indicators like walking pace and ability to get up and down stairs (or local hills) will be encouraged during weeks 9-24 and	Building confidence Promoting autonomy Building intrinsic motivation Enjoyment (meeting hedonistic needs) Building group cohesion /relatedness internal to the group Building social support and approval /relatedness external to the group Providing opportunities to give something back and support others /relatedness external to the group Presenting models of effective engagement in exercise /physical activity. . Self-regulation (planning, self-monitoring, reviewing progress, updating plans)

	beyond. This may use a pedometer, diary, app /mobile phone or other forms of self-monitoring. 7) Visit by a local activity session leader /taster session (e.g. short mat bowls, line dancing, indoor curling, Tai Chi). Sessions to involve older session participants from local community and Ambassadors (when available) 8) Breaking bad and making new habits (based on the SkiM model /intervention resources) 9) Visit to local activity session (e.g. short mat bowls, line dancing, indoor curling, Tai Chi) 10) Getting support (focus on building support networks and approval external to the programme, encourage buddying and /or ambassador involvement for people with limited social networks) 11) Becoming an ambassador (Including visit from existing ambassadors when available) 12) Managing illnesses that get in the way of your activity programme (e.g. arthritis, diabetes, back pain, heart problems) 13) Visit to local activity session (e.g..chair aerobics, Zumba Gold, social dance, short led walk) 14) Managing slips and lapses (including taking a series of session breaks for people who develop a sustained illness lasting more than 2 weeks, or who have an operation) 15) Keeping going: What stops people from being able to sustain exercise and physical activities in the long run? Discussion focused around sources of "tension" and ways to manage or remove these sources. 16) Community based physical activities– what's available and happening in your local area 17) Revisiting your goals 18) Reviewing progress and problem-solving (in every session from 10 onwards) 19) Reflection on benefits experienced to date (including self-concept related benefits) 20) Wrap up session. Planning your next steps Each study site will have the flexibility to adapt the ideas on local activity opportunities based on local resources and participant suggestions	Problem-solving /reducing barriers to increase self-efficacy /competence Habit formation Promoting positive changes in self-concept (physical, control /competence, social) Building outcome expectancies and experience of benefits .

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Appendix 3 Control group social and educational sessions

REACT Health Education programme (Control group)

Objectives	The REACT control group will receive a socially active Health Education programme with the goal of providing positive experiences and promoting engagement and retention. These social and educational materials and sessions are designed to educate participants about the benefits of healthy eating and other health-related behaviours, and maximise enjoyment, social interaction, and group identity. In addition to healthy eating, the focus will be on a variety of healthy ageing topics, including disease prevention, health care, and availability of local social opportunities.
Mechanisms of Change	Self-Determination Theory Three psychological needs motivate people to initiate and sustain behaviour. These needs are said to be universal and innate and include the need for

	competence (feeling capable and confident), autonomy (feeling in control), and psychological relatedness (feeling part of something bigger). In the case of the control group, we aim to promote the behaviours of engaging with REACT data collection events at baseline 6, 12, and 24 months, and also to increase Control Group participants' awareness of various health topics and enhance their social engagement in local activities offered for older adults.
Key Competencies	Health Education booklets: all health education booklets will adhere to the principles of Plain English, with both the language and layout designed to optimise readability, and will be tailored to meet the needs of literacy- and ethnically-diverse older adults. Health education sessions: Select members of the research team and from our local delivery partner organisations will be trained in the key competencies required to deliver sessions in accordance with Self-Determination Theory: Active Listening ("Attending") and Empathic Communication Asking Open-Ended Questions Paraphrasing Giving and Receiving Feedback Handling Emotions Summarizing Problem-Solving Group Leadership Skills Dealing with the Difficult/Challenging Participant
Materials/Sessions	
Education Only	**Weeks 1-2 after completion of baseline assessments:** 1) A booklet focusing on social events and activities in the local community will be developed by the REACT research team, in collaboration with our local delivery partners and appropriate third sector and community-based organisations who engage with adults over 65 years of age (e.g., Age UK Birmingham, Westbank, BANES Council, Golden Oldies, LinkAGE, Age Action Alliance, Brunelcare, St Monica's Trust, Contact the Elderly, etc.) 2) A booklet focusing on healthy eating will be developed by Professor Janice L Thompson (lead at the Birmingham site), and will be evidence-informed and include information on food groups and eating behaviours that promote healthy ageing, and will be consistent with national nutrition guidelines. Both booklets will be sent to all control group participants via the post within a week of completing baseline data collection measures.
Social and Education	**Month 7** 60 min
	Content

	At this session, participants will receive information on a variety of healthy ageing topics including prevention and health care: 1) Disease prevention and treatment 2) Dietary supplements: What are you taking and why? 3) Preventative medicine: Good health habits across the lifespan 4) Illness, disease knowledge and treatment 5) Did you sleep well last night? 6) Safety proofing your home Each study site will have the flexibility to choose their own topics based on local resources and participant suggestions	
	Month 13 60 min	
	Content	
	At this session, participants will receive information on a variety of local social activities, including: 1) Community resources – what's available and happening in your local area 2) Visit to local social activity session (i.e, choir, music session, art group) Each study site will have the flexibility to choose their own topics based on local resources and participant suggestions.	
	Month 25 45 min	
	Content	
	At this session, participants will be provided with more information about health and wellbeing, with the focus on engaging them in physical activities. Information and materials will include: 1) A focus on active living and the importance of maintaining functional ability. 2) Dissemination of taster session vouchers for physical activities in their local community.	

Appendix 4 Sample physical activity sessions

REACT - Sample Physical Activity Session Outline

Components of training

The physical activity program will include aerobic, strength, flexibility, and balance training. We will focus on **walking** as the primary mode of physical activity for preventing/postponing the primary outcome of major mobility disability, given its widespread popularity and ease of administration across a broad segment of the older adult population. Other forms of endurance activity (e.g., stationary cycling) are utilized when regular walking is contraindicated medically or behaviorally. Each session is preceded by a brief warm-up and followed by a brief cool-down period. In light of current clinical guidelines, participants are instructed to complete **flexibility** exercises following each bout of walking. Moreover, three times per week, following a bout of walking, participants are instructed during the initial phase of the program to complete a 10-minute routine that focuses primarily on **lower extremity muscle strengthening. Balance training** is also performed. In addition, the intervention will involve encouraging participants to increase all forms of physical activity throughout the day. This may include activities such as leisure sports, gardening, use of stairs as opposed to escalators, and leisurely walks with friends.

Intensity of training. The participants will be introduced to the intervention exercises in a structured way such that they begin with **lighter intensity and gradually increase intensity** over the first 2-3 weeks of the intervention. We will promote walking for physical activity at a **moderate intensity**. We will rely on **ratings of perceived exertion** and physical activity heart rate as a method to regulate physical activity intensity. Using Borg's scale, that ranges from 6 to 20, participants are asked to walk at an intensity of 13 (activity perception SOMEWHAT HARD). They are discouraged from exercising at levels that approach or exceed 15 (HARD) or drop to a rating of 11 (FAIRLY LIGHT) or below. Heart rate will be monitored weekly during the walking phase of the program to confirm the target training intensity. A set of lower extremity strengthening exercises are performed (2 sets of 10 repetitions) at an intensity of 15 to 16 using Borg's scale for the strength training component of the program.

Frequency and duration of training

The intervention will build to a general weekly walking goal of 150 minutes. This is consistent with the public health message from the UK Chief Medical Officer (CMO) that report that moderate physical activity should be performed for 30 minutes on 5 days a week (150 total minutes). This goal is **approached in a progressive manner** across the first 3 months of the trial. There are multiple ways that the goal can be achieved, based on the physical abilities and constraints of each participant.

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. During the early Adoption phase (weeks 1–12) each intervention participant will receive one 45-minute individualised, face-to-face introductory session, and two 60 minute physical activity sessions per week, plus 15-20 minutes social time, delivered by the REACT trainer. During weeks 12–52 session frequency will be reduced to one per week but with an expectation that

participants find an hour per week to exercise at home, in the neighbourhood or at a local physical activity session.

Home Based Training sessions

Participants are instructed from the very first physical activity session on how to plan and implement home/community based exercising

Physical environment: The physical space to accommodate the strength training component of the intervention should be an open space of approximately 400 sq. ft. The space will need to accommodate chairs, participants and equipment. There should be enough space between chairs so that participants can hold their arms out to the sides without touching one another. A sturdy chair and a medium bath towel are needed for each participant. The ideal chair should have a firm seat with no arms and the chair should be high enough so that when participants sit all the way back, their feet barely touch the floor. The back of the chair should be high enough so that participants can hold onto it while standing behind it. The towel can be placed under the knees during the seated knee extension exercises to raise the participant's feet off the floor.

Sample Training Programme

A typical physical activity session will consist of a 5-min warm-up consisting of low intensity walking (Rating of Perceived Exertion Borg scale (RPE) < 9) or, when walking cannot be performed at an RPE <9, stationary cycling. Participants then complete walking and strength training at the target RPE for each activity for the amount of time prescribed. As stated above the duration and intensity of each session generally will depend on the individual's capabilities and the phase of the study they are in. In general each session is that time required to obtain one-quarter or one-third of the total weekly prescribed. However, the duration can be modified as needed based on participant scheduling issues or problems that require adjustment. At intervals throughout the training session participants are asked to assess their RPE. At the end of each physical activity session there will be 3 minutes of cool down which will consist of gradually reducing the walking speed.

Strength training component

Strength training will focus primarily on five lower extremity exercises. Variable weight ankle weights are provided to all subjects. The goal is that the strength training component is performed three times per week during all phases of the intervention.

Specific strength training exercises

- Wide Leg Squat
- Standing Leg Curl (with ankle weights)
- Hip extension (with ankle weights)
- Bent leg raise
- Knee Extension (with ankle weights)
- Knee extension with ankle circles (with ankle weights)
- Side Hip Raise (with ankle weights)
- Leg circle

Toe Stand

Toe out calf raise

Intensity and progression:

For each strength exercise the subjects are instructed to perform 10 repetitions (1 set), rest for 1 minute and then perform a second set. For the leg curl, knee extension, and side hip raise exercise, the participants are instructed to perform each set of ten and then alternate legs. This will minimize the total time to perform the strength training exercises without compromising the quality of the program. The intensity and progression of the strength training program are monitored using the rating of perceived exertion (RPE) scale. Subjects are educated in the use of the RPE scale and report their individual RPE at the end of each exercise. For the strength training exercises, the participants should be instructed to report a "localized" RPE for the muscle groups involved in the particular exercise.

Selection of appropriate weight and progression: For each strength exercise that uses the ankle weights (leg curl, hip extension, knee extension, knee extension with ankle circles, side hip raises), the appropriate starting weight is determined by the study interventionist. At the start of a participant's physical activity program they will be given a pair of ankle weights to use for training. Initially the ankle weights will contain a small amount of weight (**3 lbs for men and 2 lbs for women**). During the introduction to the strength training portion of the physical activity intervention, the interventionist will orient the subject to strength training and begin with weight settings that are "light" (RPE 10 to 11) and easy for the subject to accomplish. In addition, participants are instructed NOT to use their ankle weights during walking or in the performance of regular household activities. They should only be worn for the strength training exercises. Participants should also be advised to wear comfortable clothing when performing their strength training exercises and that a comfortable pair of socks is advisable to prevent the development of skin irritation around the lower leg where the ankle weights are attached.

It is imperative for participants to complete the strength training at the proper intensity to maximize the training benefits. Intensity can be gauged using the RPE Scale. This scale ranges from 6 to 20 and is used to rate the difficulty of lifting a given weight. The participants should report a local RPE for the active muscle groups performing the exercise. The rating is determined for each exercise after completion of the second set of 10 repetitions.

During the first week, subjects should be encouraged to complete each strength exercise with weights that they can lift at least ten times with little difficulty ("LIGHT", RPE 10-11). If any of the exercises seems too difficult (e.g., if 10 repetitions cannot be completed), then the weight is too heavy and should be reduced.

During week 2, subjects will have the difficulty of each exercise reassessed using the current training weights. The RPE reported will be evaluated by the intervention staff together with the subject. For exercises in which the RPE has dropped below 10, a small increment in weight will be made to achieve an RPE of 12-13 ("SOMEWHAT HARD").

In week 3 the exercises will be reassessed and the weight increased to achieve an RPE of 13-14. Again, this increase in intensity may be prolonged at the discretion of the exercise interventionist depending on the adaptation of each participant to the strength exercises.

Finally, in week 4 the exercises will be reassessed and the weight increased to achieve an RPE of 15-16. Again, this increase in intensity may be prolonged at the discretion of the exercise interventionist depending on the adaptation of each participant to the strength exercises.

Proper breathing techniques are essential for the safe and appropriate performance of the strength training exercises. Subjects should be instructed to avoid holding their breath and/or performing the "Valsalva maneuver" during training. Subjects are instructed to breathe through their mouths continuously and regularly throughout the exercises. This can be done in one of two ways. First, participants may count out loud to keep the pace of the exercises. Talking (counting) ensures that participants are not holding their breath. The second method entails inhaling before the lift, exhaling through the mouth while lifting, often referred to as "exhale during the exertion," and inhaling through the nose during the lowering phase.
It is important for participants to start out at an easy level for all of these exercises. When the weight is light, the participant can safely learn the correct form of each strength exercise and learn how to breathe properly. After mastering proper technique, the participants can start to progress and meet the appropriate intensity for an effective workout.

SAMPLE STRENGTH EXERCISES

Wide Leg Squat
Starting position:
Participant stands with their feet slightly greater than shoulder-width apart about 6-8 inches in front of a chair with their arms crossed in front of their chest with shoulders relaxed.

The move:
Leaning slightly forward at the hip, participant aims their buttocks into the chair and slowly lowers themselves back to a seated position. During this exercise, keep their chest up (lifted) and their back, neck, and head in a straight line.

Pause for a breath in the seated position.

Leaning slightly forward, they should stand up slowly, making sure to keep their knees directly above the ankles. As they do this, they should push up from their heels through their lower legs, thighs, hips, and buttocks, which will help keep their knees from moving in front of their feet.
Participant repeats for a total 10 squats then pauses for a rest.
Participant completes 1 more set of 10 wide leg squats.

Notes for the study interventionist:

Participants should be sure to keep their chests lifted throughout the move, so that the body doesn't curl forward. Eyes should be looking straight ahead rather than down at the floor. If participants are experiencing any pain in their knees, interventionists should guide their technique to make sure they are not letting their knees move forward past their toes during the move and that the lower leg stays perpendicular to the floor. It is important to remind participants not to sit down in the chair completely. In addition, participants should be reminded to lower their bodies in a slow controlled manner during this exercise.

Make sure participants:

- Lean just slightly forward when beginning the move
- Don't allow their knees to come in front of their toes
- Tighten their abdominal muscles
- Don't hold their breath

STRENGTH EXERCISE 2: Standing leg curl (with ankle weights)

Starting position:
Participant stands with their feet slightly apart behind a chair with their hands gently resting along the top of the chair back for balance. They are then instructed to shift their body weight to their left leg.
The move:
Keeping their thighs side-by-side, participant slowly lifts their right foot up towards their buttocks until their upper and lower leg form a ninety-degree angle.

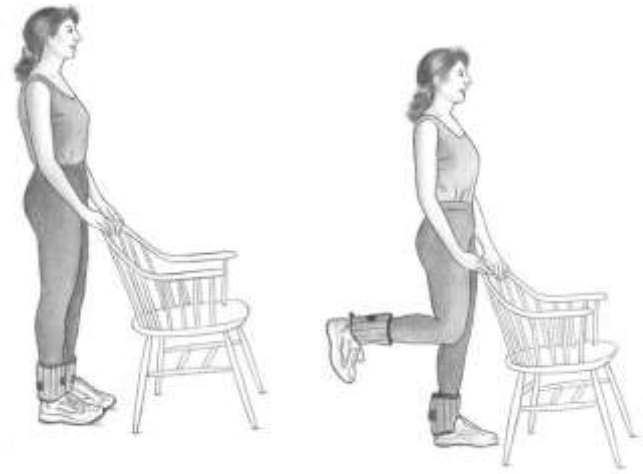
Pause for a breath.

Slowly lower their right foot back to the ground. Repeat for a total of 10 times.
Shift weight to their right leg and perform the move 10 times with their left leg.
Participant completes 1 more set with right leg and then 1 more set with left leg.

Notes for the study interventionist:

Make sure the participants:

- Keep thighs and hips even and knees touching
- Don't arch their backs as they do the exercise
- Don't let the knee or thigh move forward as the lower leg curls up
- Don't hold their breath



STRENGTH EXERCISE 2: Hip Extension (with ankle weights)

Starting Position:

Participant stands with their feet slightly apart behind a chair with their hands gently resting along the top of the chair back for balance. They are then instructed to shift their body weight to their left leg.

The move:

Breathing in slowly, then breathing out and slowly lift right leg straight back without bending the knee or pointing the toes. Participant tries not to lean forward and the left leg should be slightly bent.

Hold position for 1 second.

Breathe in as the right leg is slowly lowered back to the ground.

Repeat for a total of 10 times with their right leg.

Participant shifts weight to their right leg and performs the move with left leg.

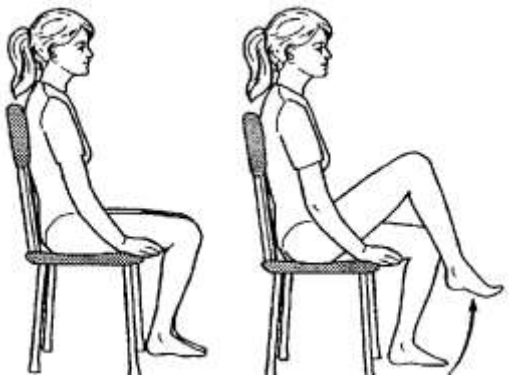
Repeat for a total 10 times with their left leg.

Participant completes 1 more set of 10 repetitions with their right leg and then 1 more set of 10 repetitions with their left leg.

STRENGTH EXERCISE 2: Hip Flexion (with ankle weights)
Starting Position:
Participant stands with their feet slightly apart behind a chair with their hands gently resting along the top of the chair back for balance. They are then instructed to shift their body weight to their left leg.
The move:
Slowly bend their right knee toward chest, without bending waist or hips.
Hold position for 1 second.
Slowly lower their right leg all the way down. Pause.
Repeat for a total 10 times with their right leg.
Shift body weight to their right leg. Perform the move with their left leg.
Repeat for a total 10 times with their left leg.
Participant completes 1 more set of 10 repetitions with their right leg and then 1 more set of 10 repetitions with their left leg.

STRENGTH EXERCISE 2: Bent Leg Raise (alternative to standing hip flexion)
Starting position:
Participant is to sit back in a chair with their feet shoulder-width apart and knees slightly separated and directly above their feet.

The move:
Participant is to raise their right knee as high as possible while keeping the knee bent.
Slowly lower their right leg back down to the chair. Pause.
Repeat for a total 10 times with their right leg.
Participant then performs the move with their left leg.
Repeat for a total of 10 times with their left leg.
Participant completes 1 more set of 10 repetitions with their right leg and then 1 more set of 10 repetitions with their left leg.



STRENGTH EXERCISE 3: Knee Extension (with ankle weights)

Starting position:
Participant is to sit back in a chair with their feet shoulder-width apart and knees slightly separated and directly above their feet. A rolled towel can be placed beneath the knees for comfort and to allow full range of motion during the exercise, as the toes should just brush against the floor when extending the leg.

The move:
Keeping their foot flexed, slowly raise their right leg until it is fully extended, with the knee as straight as possible.
Pause for a breath.
Slowly lower their right leg back to the ground.
Repeat for a total 10 times with their right leg.
Participant then performs the move with their left leg.
Repeat for a total 10 times with their left leg.
Participant completes 1 more set of 10 repetitions with their right leg and then 1 more set of 10 repetitions with their left leg.

Notes for the study interventionist:

Make sure participants:

Don't arch their backs

Straighten their legs as far as possible at the end of the lift – the last part of the muscle contraction is the most important

Don't hold their breath

STRENGTH EXERCISE 3: Knee Extension and Ankle Circles (with ankle weights)

Starting position:
Participant is to sit back in a chair with their feet shoulder-width apart and knees slightly separated and directly above their feet. A rolled towel can be placed beneath the knees for comfort and to allow full range of motion during the exercise, as the toes should just brush against the floor when extending the leg.

The move:
Keeping their foot right foot flexed, slowly raise their right leg until it is fully extended.
With their right knee as straight as possible, rotate the right ankle 5 times to the right, and then 5 times to the left.
Slowly lower their right leg all the way down. Pause.
Repeat for a total 10 times with right leg.
Participant then performs the move with their left leg.
Repeat for a total 10 times with their left leg.
Participant completes 1 more set of 10 repetitions with their right leg and then 1 more set of 10 repetitions with their left leg.

STRENGTH EXERCISE 4: Side Hip Raise (with ankle weights)

Starting position:

Participant stands straight with feet together and hands gently resting on the back of a chair for balance.

The move:
Keeping their toes pointed straight ahead; slowly lift their right leg out to the side until their foot is 5-8 inches off the ground. Do not lock the knee on the supporting leg.
Pause for a breath.
Slowly lower the right leg back to the ground.
Repeat for a total of 10 times with right leg.
Participant then performs the move with their left leg.
Repeat for a total 10 times with their left leg.
Participant completes 1 more set of 10 repetitions with their right leg and then 1 more set of 10 repetitions with their left leg.

Notes for the study interventionist:
Make sure participants:
Keep their torsos upright during this exercise, not leaning to one side
Raise their legs no more than 12 inches off the ground
Keep their fingertips on top of the chair for balance
Don't hold their breath

STRENGTH EXERCISE 4: Leg Circles

Starting position:
Participant stands straight with feet together and side toward back of chair. Have right hand gently resting on the back of a chair for balance.
The move:
Keeping foot flexed, slowly lift right leg until foot is 5-8 inches off the ground. Make a large circle clockwise while keeping the foot lifted and leg extended. Do not lock the knee on the supporting leg.
Repeat for a total of 5-10 circles with the right leg.
Slowly lower the right leg back to the ground.
Participant then performs the move with their left leg.
Repeat for a total of 5-10 clockwise circles with the left leg.
Slowly lower the left leg back to the ground.
Participant then completes 5-10 counterclockwise circles with their right leg and then 5-10 counterclockwise circles with their left leg.

STRENGTH EXERCISE 5: Toe Stand

Starting Position:

Participant stands straight with feet together and hands gently resting on the back of a chair for balance.

The move:
Participant slowly raises their body as high as possible on the balls of their feet.
Pause for a breath.
Slowly lower their heels back to the ground.
Repeat for a total of 10 times.
Participant completes 1 more set of 10 repetitions.

Notes for the study interventionist:

Make sure participants:

- Maintain good upright posture
- Do the toe stands slowly—many people have a tendency to raise and lower themselves too quickly
- Don't hold their breath

STRENGTH EXERCISE 5: Toes Out Calf Raise

Starting Position:

Participant stands behind chair with feet slightly apart then points their toes out to the side. Hands are gently resting on the back of a chair for balance.

The move:

Participant slowly raises their body as high as possible on the balls of their feet.
Pause for a breath.
Slowly lower their heels back to the ground.
Repeat for a total 10 times.
Participant completes 1 more set of 10 repetitions.

Cool-down

Hamstring & Calf Stretch

Stand facing a sturdy chair.

Slowly bend forward at the hip, keeping their legs straight without locking their knees. Rest your hands on the seat of the chair with their elbows slightly bent, feeling a stretch in the back of their upper and lower leg. Keep your back flat.

Hold the stretch for a count of 20-30 seconds.

Quadriceps Stretch

Stand next to a sturdy chair with their feet about shoulder-width apart and their knees straight – but not locked.

Hold onto the chair for balance with their left hand. Bend their right leg back and grab their right foot or ankle in their right hand until their thigh is perpendicular to the ground. Make sure they stand up straight – don't lean forward. (If they can't grab their ankle in their hand, keep their leg as close to perpendicular as possible and hold the bend.) They should feel a stretch in the front of their thigh.

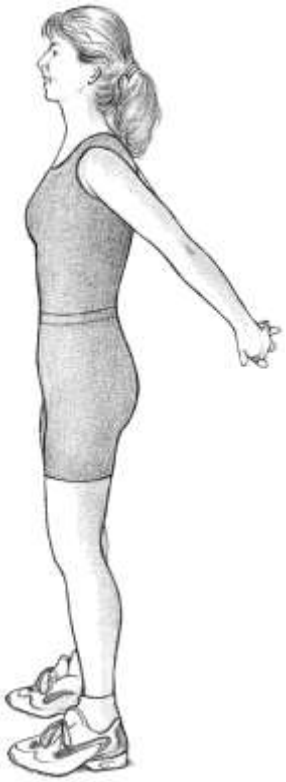
Hold the stretch for a count of 20-30 seconds, and then repeat the stretch with the other leg.

Chest & Arm Stretch

Stand with their arms down by your side.

Extend both arms behind you and clasp your hands together. Make sure their arms are straight before lifting them up behind you as high as possible. Keep their chest forward and shoulders back during the stretch.

Hold the stretch for a count of 20-30 seconds.



Upper Back Stretch

Stand (or sit) with their feet shoulder-width apart, their knees straight but not locked, and their hands clasped in front of themselves. Rotate their hands so that their palms face the ground. Then raise their arms to about chest height.

Press their palms away from their body and feel a stretch in your neck, upper back, and along their shoulders.

Hold the stretch for a count of 20-30 seconds.

Balance training component

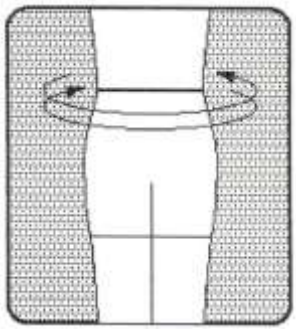
Overview:

All participants will receive the balance training begin at Level I. Participants will perform all exercises their current level. Each participant will progress to the next level of balance exercises when all exercises at that level can be performed correctly and without difficulty by the participant. Correctness of performance indicates that the exercises demonstrated to the physical activity interventionist by the participant are performed as written in the physical activity program, eight out of ten times or 3 out of five times. Difficulty might be indicated if the exercises are performed with a strained facial grimace, holding one's breath, or performance of exercises in a jerky, hesitating manner. The balance exercises are performed once a day every day.

LEVEL I BALANCE EXERCISES

Once a day

(A)



The Sink Hip Circle I

Stand facing kitchen sink

Hold on with both hands

Do not move shoulders or feet

Make a big circle to left with hips

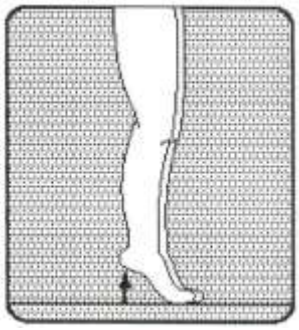
Repeat 5 times

Make a big circle to right with hips

Repeat 5 times

The Sink Toe Stand I

(B)



Stand facing kitchen sink
Hold on with both hands
Go up on your toes
Hold for count of 5
Then come down
Repeat 10 times

One Leg Sink Stand I

(C)

Stand facing kitchen sink
Hold on with both hands
Stand on your left leg for count of 5
Stand on your right leg for count of 5
Repeat 10 times

Sink Side Step I

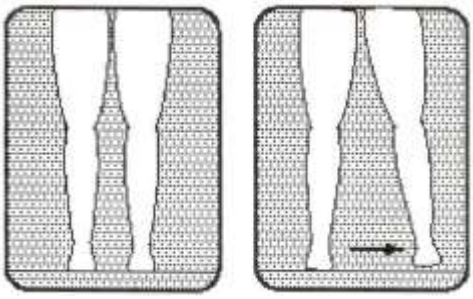
Stand facing kitchen sink

Hold on with both hands

Move hands along kitchen sink as you step to left 5 steps

Step with both feet to right 5 steps

Repeat 5 times



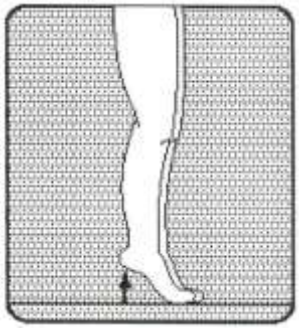
(D)

LEVEL II BALANCE EXERCISES

Once a day

The Sink Toe Stand II

(A)



Stand facing kitchen sink

Hold on with one hand

Go up on your toes

Hold for count of 5

Then come down

Repeat 10 times

One Leg Sink Stand II

(B)

Stand facing kitchen sink

Hold on with both hands

Stand on your left leg for count of 5

Stand on your right leg for count of 5

Repeat 10 times

Sink Side Step II

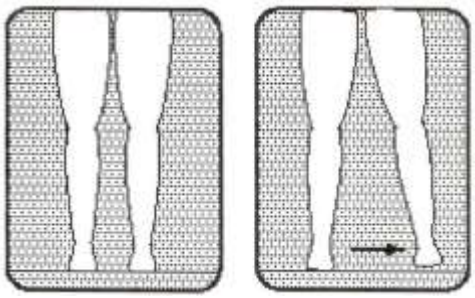
Stand facing kitchen sink

Hold on with one hand

Move hand along kitchen sink as you step to left 5 steps

Step to right 5 steps

Repeat 5 times



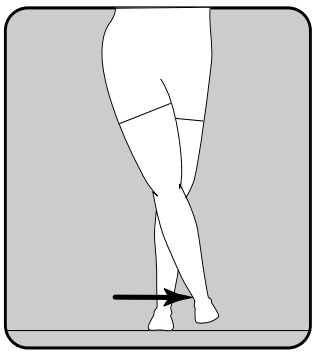
(C)

LEVEL III BALANCE EXERCISES

Once a day

Sink Leg Cross III

(A)



Stand facing kitchen sink

Hold on with both hands

Move hands along kitchen sink as you step

Cross foot in front of right foot

Take a side step with your right foot passing it out from behind your left foot

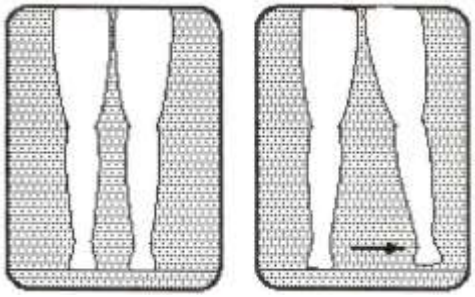
Repeat steps 4 & 5 three times

Now, cross right foot in front of left foot (reverse directions)

Take a side step with your left foot passing it out from behind your right foot

Repeat steps 7 & 8 three times

Sink Side Step III



Stand facing kitchen sink

Do not hold onto sink

Step to left 5 steps

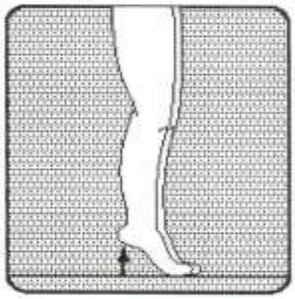
Step to right 5 steps

Repeat 5 times

(B)

The Sink Toe Stand III

(E)



Stand facing kitchen sink

Do not hold onto the sink

Go up on your toes

Hold for count of 5

Then come down

Repeat 10 times

Appendix 5 MAT-sf protocol

The Mobility Assessment Tool (short form)—MAT-sf

The MAT-sf is a 10-item computer based assessment of mobility using animated video clips. The use of animation in the videos: a) removes potential biases in judgments that may arise from characteristics such as the sex, race, age or experience of the actor, and b) standardizes item interpretation since respondents view the actual demands of the task and are no longer required to make implicit judgments regarding item content, e.g., for climbing a flight of stairs, we can present the task standardizing the speed, number of steps, light conditions and the presence or absence of handrails. The 10 items in the MAT-sf cover a broad range of functioning. The items include walking on level ground, a slow jog, walking outdoors on uneven terrain, walking up a ramp with and without using a handrail, stepping over hurdles, ascending and descending stairs with and without the use of a handrail, and climbing stairs while carrying bags. The items were selected based on individual response and information curves derived from Item Response Theory. Each item is accompanied by an animated video clip together with the responses for that question (number of minutes, number of times, yes/no). The test can be done on any laptop and scores are saved to an exportable file. The time required to do the test with instructions from the examiner is ~5 min.

In the informed consent, we describe the assessment in the following manner: “The MAT-sf is computer based physical performance test that uses animated clips rather than words to describe both the nature and demands of the tasks.” This language has been approved by our IRB. The instructions which are integrated into the test window are as follows:

1. This survey consists of 10 short video clips of different physical tasks. To watch each video, simply click the PLAY button at the bottom of each.
2. After watching each video, we would like you to tell us whether you could perform the task or in some instances how many times or for how long. To indicate your response, click the appropriate button at the bottom of the screen. Note that the video must be completed before you can enter your response.
3. Please be as honest as possible in your responses. If you have questions or are confused, be sure to ask someone for help.
4. Even if you have never done the actual tasks in the videos, please provide your best guess for each response.

To begin, put the ID that was given to you in the box below and then check START!

<u>Implementation in LIFE</u>

Because the MAT-sf is a computer software program, it will be loaded on the assessment PCs before they are distributed to the sites. The program has a very sophistication scoring template which will save each participant’s output to a scoring file and then automatically upload it to the LIFE website. If you do not have connectivity, it will save the file and upload it the next time you do have connectivity and access the program.

Content Validity

In the development of the MAT-sf, content validity was of central concern. Recall that the goal was to have a set of items that sampled the following six clusters: walking on a flat surface, walking up inclined ramps, walking while stepping over hurdles, walking outdoors uphill on uneven terrain, climbing stairs with and without handrails, and climbing stairs while carrying bags in one or both arms. In addition, we wanted to have a set of items for the MAT-sf that captured a broad range of abilities and items that provided valuable information to the measure.

Figure 2 (see attachment) illustrates that there was at least 1 item chosen from each of the clusters described previously. This figure also presents the item characteristic curves (ICC) and the information curves for the 10 items. For dichotomized items such as item 5, *stepping over low hurdles*, the ICC depicts the likelihood of positively responding to the item, in other words the ability to perform the task. For items that use an ordinal scale such as item 1 (*walking on level ground*), the number of response curves is equal to the number of categories minus 1. Each of these curves again represents the likelihood of a positive response to each of the specific categories of functional ability for that item. A steeper ICC generally suggests higher discriminating power of the item or item category at the location where the curve has its steepest slope. On the other hand, the information curve denoted by the dotted line on the right side of the scaled graph indicates the amount of information contained in each specific item. Higher information suggests more accurate estimates of ability for a particular item or category (see Figure 2 attached).

The 10 items cover the range of functional ability quite well. For example, a sequential examination of items 1, 7, 8, 9, and 2 reveals a graduated increase in the complexity and difficulty that is inherent in different forms of mobility; these items also cover a broad range of the ability continuum. Note that both items 3 and 4 tap a focal point in the middle section of the ability distribution. The tradeoff is that, despite this narrow range, items 3 and 4 have relatively high information content which tends to “stretch” the information scale for all items.

Reliability and Validity

Having identified the items for the MAT-sf, we then proceeded to examine the reliability and validity of the measure. Because we had complete data on all 79 items, we began by calculating a composite score for each participant using all items and then correlated it with scores from the 10-item MAT-sf. As desired, the two were very highly related with one another; $r = 0.96$, $p<.001$. In addition, we conducted a 2-week test-retest reliability coefficient for the MAT-sf in a sub-sample of 30 participants and found that the measure was very stable over this time period, $r = 0.93$, $p<.0001$.

Several steps were conducted to garner support for the validity of the MAT-sf. As support for convergent validity, we computed bivariate correlations between the MAT-sf and a validated self-report measure of disability, the PAT-D. Our hypothesis was that of the three PAT-D subscales—ADL, mobility, and IADL—the strongest relationship would exist between the PAT-D disability subscale and the MAT-sf, whereas the weakest relationship would be found for the IADL subscale. This is exactly what occurred in that the correlations of the MAT-sf with the mobility, ADL, and IADL subscales of the PAT-D were -.60, -.50, and -.44, respectively; all r values were significant at a

p<.001. As evidence of construct validity, we performed a known groups sex difference for the MAT-sf; as expected, we found that women (mean ±SE = 52.07 ±0.78) self reported lower ability for mobility than men (57.96 ±1.18), t (231) = 4.10, p<.001. (See Table 1 below for means and SDs of variables.)

Finally, as further evidence for the construct validity of the MAT-sf, we conducted 2 separate stepwise regression analyses, one for the SPPB and a second for the 400-M walk. In these analyses, the PAT-D mobility score was entered first followed by the MAT-sf scores. In both analyses, the entry of the MAT-sf contributed over and above the PAT-D mobility subscale to the explanation of performance-based function; for the SPPB, the change in R^2 was an additional 9.8% and for the 400-M walk it was 16.7%. The zero order correlations of the MAT-sf to the SPPB and 400-M walk gait speed were 0.59 (p<.001) and 0.58 (p<.001), respectively. It is also of interest to point out the standardized β weight for the MAT-sf was substantially larger than the PAT-D mobility subscale in both analyses, see Table 2 below.

Table 1. Descriptive Statistics for Study Measures

Measure	N	Mean ±SD
400-M walk Time (m/sec)	187	1.04 ±0.27
Short Physical Performance Battery	232	8.61 ±2.70
PAT-D: Total Score	234	0.37 ±0.42
PAT-D: ADL	234	0.25 ±0.33
PAT-D: Mobility	234	0.71 ±0.83
PAT-D: IADL	234	0.23 ±0.38
MAT-sf	231	53.78 ±10.31

*PAT-D = Pepper Assessment Tool for Disability

Table 2. Final Regression Models of PAT-D Mobility and MAT-sf on the SBBP and 400-M Gait Speed

SPPB; R^2 = 40%			
Measure	**Standardized β**	**t-Value**	**p Value**
PAT- D Mobility	-.31	-4.78	<.0001
MAT-sf	.40	6.11	<.0001

400-M Walk Gait Speed; R^2 = 37%			
Measure	**Standardized β**	**t-Value**	**p Value**
PAT-D Mobility	-.20	-2.91	.004
MAT-sf	.48	6.91	<.0001

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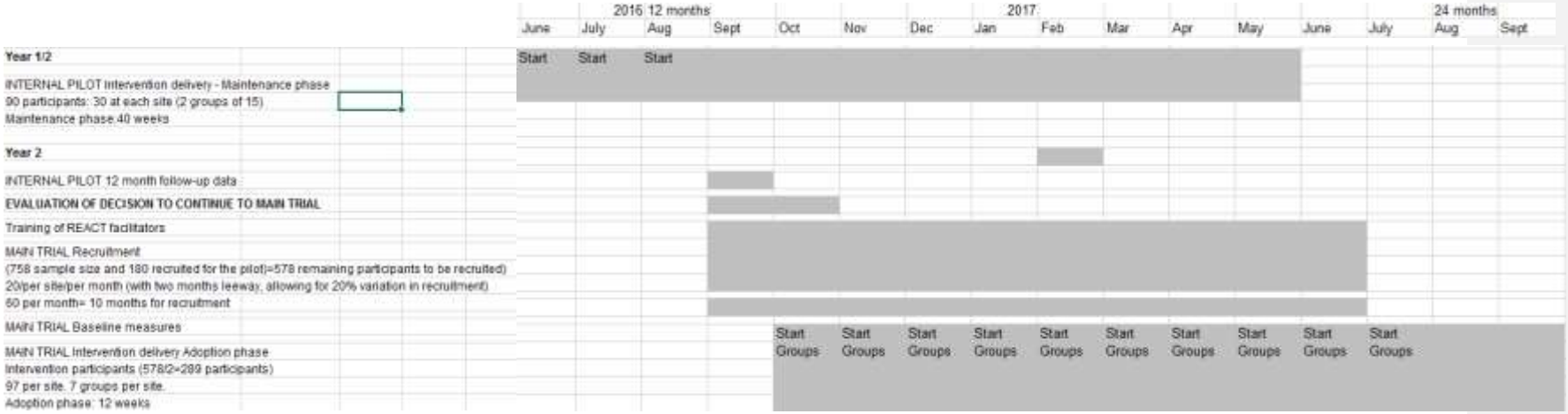
Appendix 6 Trial Project Management Plan

	2015				2016						2016	12 months	
	Sept	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	June	July	Aug	Sept
Year 1													
Funding confirmed.NIHR contracting/other	Start of study												
Study set up													
Ethics form submission													
Meetings with collaborators - identifying facilities/settings for delivery -identifying REACT specialists for each													
Research assistants appointments	Post advertised	Selection			Start/induction								
Preparing training manual for REACT specialists													
Training REACT specialists for internal pilot													
REACT Launch conference													
Identify partner practices and meet to set up recruitment procedures													
INTERNAL PILOT - Recruitment (60 people per site) x 3 sites=180 people in total for internal pilot (90 intervention-90 control)													
INTERNAL PILOT Baseline measures 90 participants: 30 at each site (2 groups of 15)													
INTERNAL PILOT Intervention delivery - Adoption phase 90 participants: 30 at each site (2 groups of 15) Adoption phase:12 weeks							Start	Start	Start				


2016 12 months
2017
24 months
June July Aug Sept Oct Nov Dec Jan Feb Mar Apr May June July Aug Sept
Year 1/2
Start Start Start
INTERNAL PILOT intervention delivery - Maintenance phase
90 participants: 30 at each site (2 groups of 15)
Maintenance phase 40 weeks
Year 2
INTERNAL PILOT 12 month follow-up data
EVALUATION OF DECISION TO CONTINUE TO MAIN TRIAL
Training of REACT facilitators
MAIN TRIAL Recruitment
(758 sample size and 180 recruited for the pilot)=578 remaining participants to be recruited)
20/per site/per month (with two months leeway, allowing for 20% variation in recruitment)
60 per month= 10 months for recruitment
MAIN TRIAL Baseline measures
Start Groups
MAIN TRIAL Intervention delivery Adoption phase
Intervention participants (578/2=289 participants)
97 per site. 7 groups per site.
Adoption phase: 12 weeks


2017
24 months
2018
36 months
Year 2/3
Jan Feb Mar Apr May June July Aug Sept Oct Nov Dec Jan Feb Mar Apr May June July Aug
MAIN TRIAL Intervention delivery - Maintenance phase
Intervention participants (578/2=289 participants)
97 per site. 7 groups per site.
(Assumption=1 group per site starts each month)
Maintenance: 40 weeks
Maintenance phase started for all groups
Completion of maintainance phase for all groups
Year 3
INTERNAL PILOT 24mo follow-up
MAIN TRIAL 12 month follow up


2019
48 months
2020 54 months
Sept
Oct
Nov
Dec
Jan
Feb
Mar
Apr
May
June
July
Aug
Sept
Oct
Nov
Dec
Jan
Feb
Year 4
MAIN TRIAL 24 month follow up
Main trial intervention participants (578/2=289 participants)
97 per site 7 groups per site
24 month follow-up
Year 5
Analysis and write up
End of study 54 month

Appendix 7 Press releases (3 versions)

University of Bath Press Release
INSERT DATE

A new multi-centre study could help older adults delay frailty and live independently for longer

A major study, led by researchers at the University of Bath, has launched to test a new approach to helping older adults maintain good physical and mental health and retain the physical function levels required for independent living for as long as possible.

Project REACT (REtirement in ACTion) targets people over 65 years old who are starting to find everyday activities such as walking, climbing stairs and getting up from a chair difficult. By engaging these people in a specially designed 12-month physical activity and social programme REACT will test whether a decline in mobility and physical function can be slowed, stopped or even reversed.

Funded by a £1.64m grant from the National Institute of Health Research, REACT is based on LIFE, a US programme which successfully proved that physical activity prevents loss of mobility in older adults. REACT will recruit almost 800 people in Bath, Bristol, Birmingham and Devon starting in February 2016 with first sessions running by April.

People over 65 years are the least active in society despite the fact that recent research shows that the most active older people need fewer prescriptions and are less likely to be admitted to hospital in an emergency. A fit and active older person has a 36% lower risk of developing disabilities and a 38% lower risk of hip fracture. There is also strong evidence that greater physical activity can help protect against cardiovascular disease, diabetes and some cancers as well as reducing the risk of depression, dementia and Alzheimer's disease.

Not only does avoiding health problems leads to a greater quality of life for older adults, it also reduces the impact on the NHS and social care services. REACT will measure whether the programme is an effective and cost-effective way to reduce health and social care costs and so benefit society as a whole. Participants will also be invited to undergo a state-of-the art fMRI scan, allowing REACT to assess the direct effect of exercise on the brain and provide robust evidence on the impact of an active lifestyle on cognitive function in later life.

REACT is a collaboration led by the University of Bath which includes the Universities of Exeter, Birmingham, West of England and Oxford. Other partners in the study include Bath and North East Somerset Council, AGE UK Birmingham and West Bank Organisation Exeter.

Chief Investigator from the University's Department for Health, Dr Afroditi Stathi, explained: "This is a unique opportunity for us to test a programme which could lead to substantial gains for both individuals and wider society. We are building on a

programme that has already been successful in the US so we are optimistic that we can deliver real benefits to the people who take part."

"What is also exciting is that we are working across England, across inner cities, suburban and rural settings to get a real understanding of whether this programme can deliver benefits for older people from all walks of life. We have built excellent relationships with our partners who support us in delivering REACT in community settings. Our long-term goal for REACT is to continue to be delivered by our partners after the end of the research phase not only for the REACT participants but for all older people who face mobility difficulties".

To find out more see http://www.bath.ac.uk/health/research/projects/retirement-in-action

Ends

To arrange interviews with _____ please contact the University of Bath Press Office on +44-1225386319 / +44-7966341431 or email press@bath.ac.uk . ISDN available for radio interviews.

Notes

We are one of the UK's leading universities both in terms of research and our reputation for excellence in teaching, learning and graduate prospects.

In the REF 2014 research assessment 87 per cent of our research was defined as 'world-leading' or 'internationally excellent'. From making aircraft more fuel efficient, to identifying infectious diseases more quickly, or cutting carbon emissions through innovative building solutions, research from Bath is making a difference around the world. Find out more: http://www.bath.ac.uk/research/

University of Birmingham Press Release
INSERT DATE

A new multi-centre study could help older adults delay frailty and live independently for longer

The University of Birmingham is one of three field centres for a major new study that will test a new approach to helping older adults maintain good physical and mental health and retain the physical function levels required for independent living for as long as possible.

Project REACT (REtirement in ACTion) targets people over 65 years old who are starting to find everyday activities such as walking, climbing stairs and getting up from a chair difficult. By engaging these people in a specially designed 12-month physical activity and social programme REACT will test whether a decline in mobility and physical function can be slowed, stopped or even reversed.

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Not only does avoiding health problems lead to a greater quality of life for older adults, it also reduces the impact on the NHS and social care services. REACT will measure whether the programme is an effective and cost-effective way to reduce health and social care costs and so benefit society as a whole. Participants will also be invited to undergo a state-of-the art fMRI scan, allowing REACT to assess the direct effect of exercise on the brain and provide robust evidence on the impact of an active lifestyle on cognitive function in later life.

REACT is a collaboration which includes the Universities of Birmingham, Bath, Exeter, West of England and Oxford. Other partners in the study include Bath and North East Somerset Council, AGE UK Birmingham and West Bank Organisation Exeter.

Professor Janice L. Thompson, REACT Principal Investigator from the University of Birmingham explained, "What is exciting about REACT is that we are working across England, within inner cities, suburban and rural settings to get a real understanding of whether this programme can deliver benefits for older people from all walks of life. We have established collaborative relationships with our community partners, who

work with diverse older adults every day and are the key to our successful delivery and evaluation of REACT in community settings."

Dr Afroditi Stathi, REACT Chief Investigator from the University of Bath, agrees. "This is a unique opportunity for us to test a programme which could lead to substantial gains for both individuals and wider society. We are building on a programme that has already been successful in the US, so we are optimistic that we can tailor the programme for the UK, and deliver it to provide real benefits to the people who take part. Our long-term goal for REACT is that it will continue to be delivered by our partners after the end of the research phase, not only for the REACT participants but for all older people who face mobility difficulties."

To find out more see http://www.bath.ac.uk/health/research/projects/retirement-in-action

Ends

For further information

Kate Chapple, Press Office, University of Birmingham, tel 0121 414 2772 or 07789 921164, email: k.h.chapple@bham.ac.uk

Notes

The University of Birmingham is a truly global University producing world-leading research and is ranked among the world's top 100 institutions. With almost 5,000 international students from more than 150 countries, Birmingham's campus is a diverse and global place which attracts the brightest and best students and staff.

University of Exeter Press Release
INSERT DATE

A new multi-centre study could help older adults delay frailty and live independently for longer

The University of Exeter is one of three field centres for a major new study that will test a new approach to helping older adults maintain good physical and mental health and retain the physical function levels required for independent living for as long as possible.

Project REACT (REtirement in ACTion) targets people over 65 years old who are starting to find everyday activities such as walking, climbing stairs and getting up from a chair difficult. By engaging these people in a specially designed 12-month physical activity and social programme REACT will test whether a decline in mobility and physical function can be slowed, stopped or even reversed.

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REACT is a collaboration which includes the Universities of Exeter, Bath, Birmingham, West of England and Oxford. Other partners in the study include Bath and North East Somerset Council, AGE UK Birmingham and West Bank Organisation Exeter.

Dr Colin Greaves, REACT Principal Investigator from the University of Exeter Medical School, (*Please feel free to add your own quote and I can edit this down and add to Afroditi's quote?*) explained "What is exciting about REACT is that it is a real chance to boost the quality of life of people in their twilight years by actually preventing disability. We are working across rural area, inner cities and suburban

settings to get a real understanding of whether this programme can deliver benefits for older people from all walks of life."

Dr Afroditi Stathi, REACT Chief Investigator from the University of Bath,agreed, "This is a unique opportunity for us to test a programme which could lead to substantial gains for both individuals and wider society. We are building on a programme that has already been successful in the US so we are optimistic that we can deliver real benefits to the people who take part. Our long-term goal for REACT is to continue to be delivered by our partners after the end of the research phase not only for the REACT participants but for all older people who face mobility difficulties"

To find out more see http://www.bath.ac.uk/health/research/projects/retirement-in-action

Ends

To arrange interviews with _____ please contact the University of Exeter Press Office on : 01392 724927 or email pressoffice@exeter.ac.uk. ISDN available for radio interviews.

Notes

About the University of Exeter Medical School

The University of Exeter Medical School is improving the health of the South West and beyond, through the development of high quality graduates and world-leading research that has international impact.

As part of a Russell Group university, we combine this world-class research with very high levels of student satisfaction. The University of Exeter Medical School's Medicine programme is ranked 11th in the Guardian University Guide 2016. Exeter has over 19,000 students and is one of the global top 100 universities according to the Times Higher Education World University Rankings 2015-16, positioned 93rd. Exeter is also ranked 7th in The Times and The Sunday Times Good University Guide 2016, 9th in the Guardian University Guide 2016 and 10th in The Complete University Guide 2016. In the 2014 Research Excellence Framework (REF), the University ranked 16th nationally, with 98% of its research rated as being of international quality. Exeter's Clinical Medicine research was ranked 3rd in the country, based on research outputs that were rated world-leading. Public Health, Health Services and Primary Care research also ranked in the top ten, in joint 9th for research outputs rated world-leading or internationally excellent. Exeter was named The Times and The Sunday Times Sports University of the Year 2015-16, in recognition of excellence in performance, education and research. Exeter was The Sunday Times University of the Year 2012-13.

www.exeter.ac.uk/Medicine

Appendix 8 Publicity materials

Are you 65 years or older and starting to have difficulty doing daily activities, such as walking, getting up from chairs, and climbing stairs?

If so you may be eligible to take part in a new research study.

If you are eligible, you may receive:
- Free access to a physical activity program focusing on walking, strength, flexibility and balance training
- Free group health education sessions with other participants, focusing on successful aging

The REACT study: REtirement in ACTion University of (Bath/Birmingham/Exeter)

For more information, call (*local RA*) on (*local phone no*) or email (*email address*)

Principle Investigator: (*Local PI*)

Appendix 9 The UK BioBank Cognitive function test overview

COGNITIVE FUNCTION WEB-BASED QUESTIONNAIRE

FOR UK BIOBANK:
HEALTHY MINDS

Executive Summary

This web-based questionnaire is concerned with using the internet to assess cognitive function. With the completion of recruitment, UK Biobank is now focused on following the cohort over time. UK Biobank has written consent from participants for re-contact for this purpose.

Decline in cognitive performance with age is an increasingly significant public health problem. UK Biobank is uniquely placed to identify the causes of cognitive change and so contribute to the discovery of prophylactic and therapeutic interventions for this widespread and distressing condition.

Cognitive function was assessed at the baseline assessment when participants were recruited. This web-based questionnaire involves repeating the baseline assessment and to add two further tests to broaden the cognitive phenotype covered in UK Biobank. Table 1 shows tests that are being repeated and tests that are being added. Tests have been selected which are related to dementia. All tests have been constructed specifically for use in UK Biobank and other epidemiological studies in order to conform to the constraints of conducting large population-based studies. All tests have been constructed using established testing paradigms that have been shown to produce valid scores and to be acceptable to participants. Two of these tests (fluid intelligence and working memory) have been previously administered using the internet and were shown not to affect their acceptability to participants.

Newly introduced tests were selected after consultation with the UKB cognitive psychology sub-group led by Dr John Gallacher (Cardiff) and including Professor Ian Deary (Edinburgh) and Professor Scott Hofer (Victoria, BC). Screen shots of the tests are given in the appendix.

Table 1: Cognitive Test Battery

Measurement status	Test	Cognitive domain	Estimated Time (Mins)	
Tests to be repeated	Reaction time	Simple Processing speed	3	
	Pairs	Episodic memory	4	
	Reasoning	Fluid intelligence	3	
	Digit recall	Working memory	4	
Tests to be introduced	Trail making	Visual attention	4	
	Digit-symbol substitution	Complex processing speed	3	

One of the baseline tests has been modified slightly to overcome a ceiling effect. A substantial proportion of participants (20%) obtained extremely high scores (0 or 1 errors) on the pairs test at baseline. To address this, the previously most difficult condition (a 3x4 matrix of stimuli) will be augmented by a new most difficult condition (4x4 matrix) for participants who score 0 or 1 errors.

An important influence on cognitive function is mood. Low mood will deleteriously affect cognitive performance. It is helpful, therefore to assess mood at time of cognitive testing. We propose to do this by administering the MHI-5 questionnaire immediately prior to cognitive testing. The MHI-5 is a widely used short questionnaire derived from the mental health scale of the SF-36. The MHI-5 items are given in table 2. A five point response scale is used for each item comprising: all of the time, most of the time, some of the time, a little of the time, none of the time.

Table 2: MHI-5 items

Item	Content
1	Been very nervous
2	Felt so down in the dumps that nothing could cheer you up
3	Felt calm and peaceful inside
4	Felt downhearted and depressed
5	Been happy

It is estimated that these tests, including the MHI-5, will take 20-25 minutes to complete. This estimate comes from experience of the baseline examination and the design constraints of the new tests. Participants may complete the cognitive tests over more than one session. Tests are accessed through the main UK Biobank website with a secure link to the individual tests which are hosted on a secure site.

Re-contact procedures are similar to those used in the web-based dietary assessment. An email will be sent to all known participant email addresses (roughly 62% of the cohort) inviting them to participate in UK Biobank's Healthy Minds project (further cognitive assessment). The email will include a link to the UK Biobank website, from which the participant will be automatically directed to a server at University of Oxford, from where the cognitive tests will be administered. The invitation email will also contain the telephone number for the Participant Resource Centre, whose staff would be trained to provide information about the cognitive testing. A reminder email will be sent to those participants who have not responded after two weeks.

Participation is entirely voluntary. For all tests there will be an option to skip the test and go on to the next test. Findings will not be fed-back to participants (in accordance with the original consent) and the data will be used for research purposes only.

Post-summary: This questionnaire was administered between Dec 2014-Feb 2015 to all 340,000 UK Biobank participants with an email address, with a reminder email sent to non-responders. Overall, a total of 143,000 participants completed at least one of the tests and 120,000 completed all of them. This data will be made publicly available for UK Biobank researchers to request for research that is deemed to be in the public interest.

1. Paired associates learning task

For this task, a 3x4 matrix of cards is presented and then covered. The task is to remember the position of identical pairs within the matrix.

The instructions are:

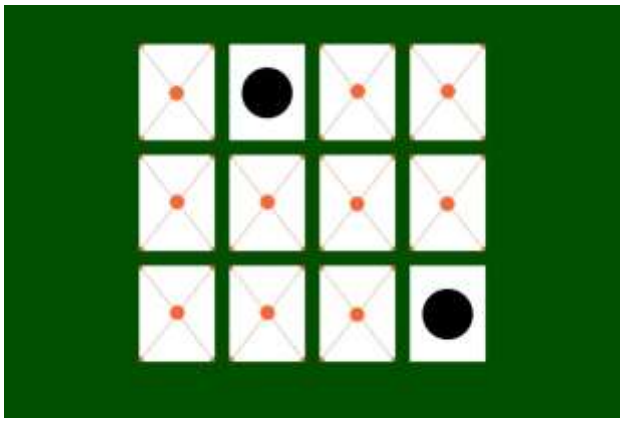
"First, we'd like you to play a game of Pairs. In this section you will be shown a set of picture cards. Please try to remember as many of them as you can. The pictures will then be turned over. Please identify each pair of pictures by clicking them on the screen. Please continue until all the pairs have been correctly identified."

A maximum number of 50 attempts is allowed after which the test is terminated.

The score is the number of attempts required to correctly identifying the location of all pairs in the matrix. Participants who score 6 or 7 (perfect and near perfect scores) will be presented with a 4x4 matrix to avoid ceiling effects.

Figure 1

Screen shot of paired associates learning task



2. Stop-Go reaction time task

For this task, pairs of cards are presented and a response is made (hitting the space bar) when the cards are the same.

The instructions are:

“We would now like you to play a game of snap. Two picture cards will be presented. When the cards are the same press the space bar as quickly as you can.”

The score is the average reaction time for the correct responses.

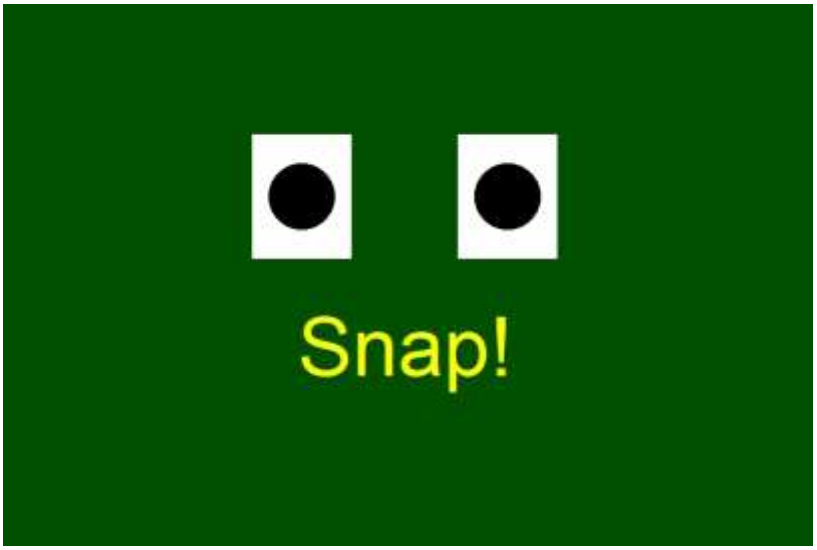


Figure 2

Screenshot of reaction time task

3. Fluid intelligence task

For this task, a series of verbal and numerical logical questions are asked. Each question has five answers to choose from.

The instructions are:

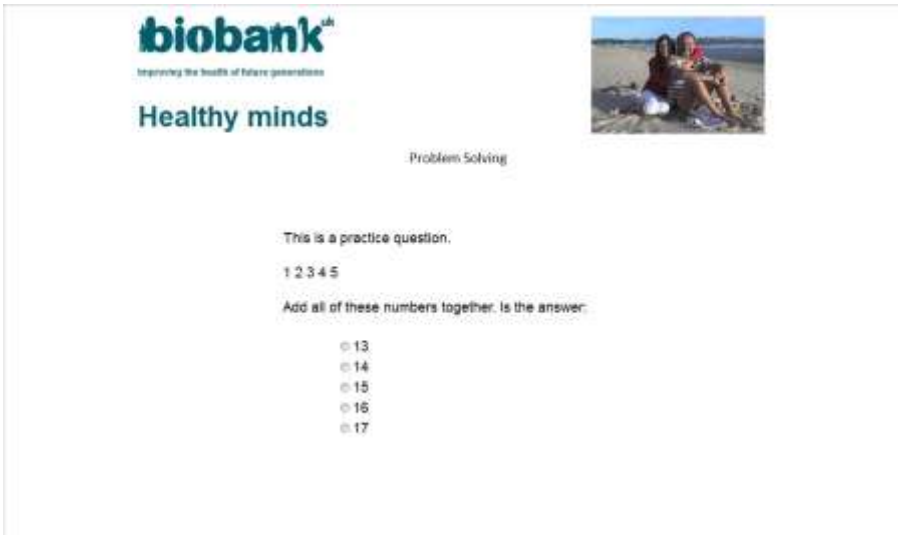
“We now would like you to solve some puzzles. You will have a maximum of two minutes to answer as many questions as possible. Don’t spend too long on any one question and you can skip any question if you wish.”

The score is the number of correct answers provided within two minutes.

An example numeric question is given below.

Figure 3

Screen shot of Fluid intelligence task



4. Working memory

For this task a series of numbers are presented and then covered. The series of numbers has to be correctly recalled. The length of the series increases with successful recall.

The instructions are:

“This is a memory challenge. We will show you a number to remember and then hide it. After a short wait, we will ask you to enter the number in reverse using the number pad on the screen. The numbers will grow longer as the test continues.”

The test is terminated after two incorrect attempts at given sequence length.

The score is the longest sequence of digits correctly recalled.

Figure 4

Screenshot of working memory task

5. Trail-making test

For this task circles must be linked in numeric order. Linkage is made using a computer mouse by clicking the next circle. There are two presentations: one using numbers and one using numbers and letters.

The instructions are:

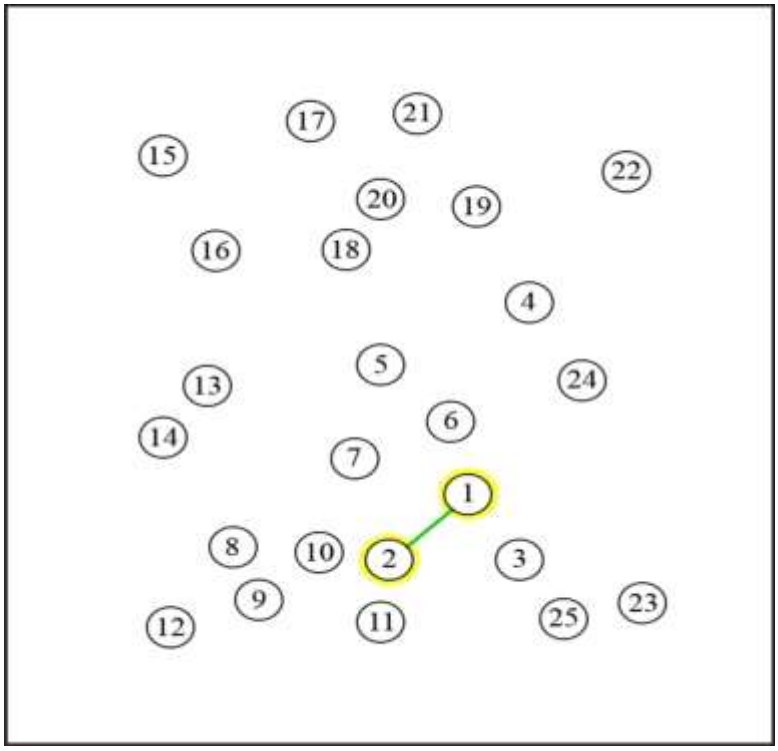
“We now want to measure your coordination. Beginning with number 1, join all the circles in numeric order by clicking over the next numbered circle using the mouse. Please work as quickly and accurately as you can.”

Only correct answers are accepted, but incorrect answers are recorded.

The score is the time taken to correctly link all the circles.

Figure 5

Screenshot for trail-making task



6. Digit-symbol substitution task

For this task, symbols must be replaced with numbers using the number pad provided.

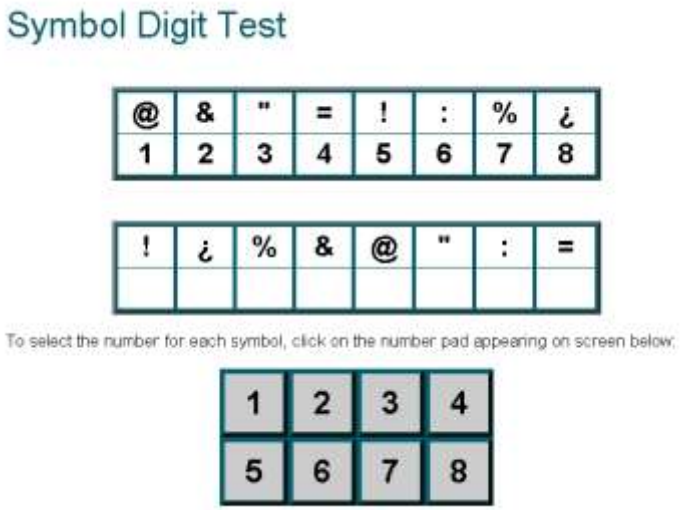
The instructions are:

“This is a code-breaking game. A code is given at the top of the page linking a symbol to a number. In the bar at the bottom of the page, place the correct number in the box under each symbol according to the code. Working from left to right select the correct number using the number pad on the screen. Please work as quickly and accurately as you can. You will have two minutes to do as many as you can”

The score is the number of correctly completed boxes.

Figure 6

Screenshot of digit-symbol substitution task



Appendix 10 REACT Process evaluation plan

REACT process evaluation plan

This document is a process evaluation plan for the REACT randomised controlled trial. In developing this document, account has been taken of the recommendations outlined in the MRC guidance on process evaluation.

Section 1 outlines key points from the MRC guidance that have been considered. Section 2 describes a logic model for REACT which provides a basis for the process evaluation. Section 3 provides the hypotheses tested in the process evaluation. Sections 4 and 5 summarise plans for the process evaluation, including both qualitative and quantitative data collection. Section 6 provides the topic guides for the qualitative evaluation and section 7 provides a list of references.

1. Background: The MRC process evaluation guidance

MRC process evaluation guidance advises that the starting point to design a process evaluation is to clearly specify the causal assumptions underlying the intervention and its implementation. That is, a clearly articulated logic model is required at the outset. This will enable the process evaluation to investigate the plausibility of the logic model by examining the relationships specified.

The purposes of process evaluation in the REACT trial are to:

- evaluate the feasibility of implementation and to inform intervention design and evaluation
- evaluate the quality and quantity of intervention delivery to inform conclusions about intervention effectiveness
- investigate the proposed mechanisms of change, outlined in the logic model and to seek alternative explanations if this model is not supported
- understand the role of context to inform whether and how the findings can be generalised

1.1 Content of process evaluations

Fidelity, dose

An intervention might not 'work' because it was not well designed or because it was not properly implemented. It might work, even if it was not implemented as intended. Therefore, a process evaluation should capture:

- whether the intervention was delivered as intended (fidelity)
- how much of the intervention was delivered (dose)

Adaptations can be made to the implementation of an intervention which enables it to fit different contexts and a process evaluation can help identify which of these adaptations might undermine or enhance effectiveness.

Delivery methods

Understanding the means of delivering an intervention through process evaluation can inform how the intervention can be replicated in the 'real world'. These means include the provision of training, communication, management, implementers attitudes and the relationship between these factors.

Reach

Process evaluation can also investigate whether and how participants come into contact with the intervention and how generalisable the intervention is (or is likely to be) in different contexts.

Mechanisms

To understand the causes of effects from an intervention requires identification of the mechanisms by which change is achieved. Process evaluation can test whether the theory about an intervention's causal pathways (as articulated by a logic model) 'works'.

Context

Factors external to the intervention can potentially act as a barrier or facilitator to implementation or to its effects. Implementation or mechanisms might also need to be adapted to these contexts to enable the intervention to work. Equally, implementation might not vary but the effect of the intervention will vary depending on context. Process evaluation can be used to understand contexts and their relationship with implementation, mechanisms and effects (e.g. whether ethnicity moderates intervention effectiveness).

Process evaluation research questions

It is not realistic for a process evaluation to address all aspects of the implementation of an intervention. It is preferable to provide satisfactory answers to the most important questions than to inadequately address too many questions. To identify the key questions, it is necessary to identify the causal assumptions of the intervention model and which of these have the most limited evidence base. Further research questions might arise during the implementation process - therefore a process evaluation should be flexible in order to respond to emerging questions.

1.2 Implications of MRC guidance for the REACT process evaluation

In developing the plan to carry out a process evaluation of REACT, clarity is needed about:

- The purposes of the process evaluation (research questions)

- The logic model and which elements of it that the process evaluation will address
- Which elements of implementation the process evaluation will address (e.g. fidelity, dose, delivery methods, reach)
- The extent to which context and mechanisms will be investigated
- The methods required to address the research questions

The remainder of this plan covers these issues.

2. The REACT logic model

2.1: Theoretical basis for the REACT intervention

The REACT social /education programme will be largely informal and aimed at maximising social interaction and enjoyment. However, it will contain some structured elements designed to teach participants skills that will help them to plan, implement and maintain a healthy level of physical activity, as well as the muscle-strengthening /function-sustaining exercises that they learn in the exercise sessions.

The REACT social programme draws on the following, overlapping (and mutually compatible) theoretical perspectives. Social Cognitive Theory and Self Determination Theory provide the main principles and processes for supporting behaviour change. The Skills for Maintenance (SkiM) model (below) has been used to identify additional processes and techniques to promote maintenance of physical activity /exercise.

Social Cognitive Theory[1 2]

People can learn by observing others and the consequences of their actions, as well as by getting feedback on their own actions. Learners can acquire new behaviours and knowledge by observing and copying a model (another person), especially if they identify positively with the model. This overlaps to some extent with the concept of “relatedness” in Self-Determination Theory (below).

People set goals for themselves based on outcome expectancies (expectation of benefit) and self-efficacy (perceived ability to achieve the behaviour) and direct their behaviour accordingly. They are then motivated to continue a new activity to the extent that they get positive feedback about a) benefits and dis-benefits of doing the activity (outcomes) and b) their experienced ability to master /achieve the new behaviour (self-efficacy).

The process of behaviour change /maintenance is cyclic, with positive outcomes and the building of self-efficacy, as well as environmental factors acting to reinforce continuation. This process of self-regulation or “learning from experience” requires time for learning of new behaviours to be embedded.

Self-Determination Theory[3-5]

Three psychological needs motivate people to initiate and sustain behaviour. These needs are universal and innate and include the need for competence (feeling capable and confident), autonomy (feeling in control of decisions /goals, having motivation that is intrinsic (self-generated)), and relatedness (social engagement, social acceptance /approval of the behaviour, giving support to others). Fulfilling these needs through engagement in a social physical activity programme may lead to an improvement in the social and control /competence domains of the self-concept.[6]

The Skills for Maintenance (SkiM) model[7]

This new model focuses on the skills that people need to maintain lifestyle changes. The main premise is that changing your lifestyle can induce psychological and social tensions in your life. The sources of tension for physical activity may include conflict with other priorities, the needs of others, discomfort /lack of enjoyment associated with the new activity, conflict with established habits, or conflict with established beliefs /self-concept (habits of thinking). This tension can be managed in the short term through willpower, self-regulation and regular re-motivation, as well as by making plans to manage any slips and lapses that occur. However, to achieve long-term change requires individuals to either pre-empt and prevent the tension (make changes you can live with /will enjoy), or to resolve it by finding other ways to address the sources of the tension (e.g. to negotiate to resolve conflicts with the needs of others; actively challenge and change unhelpful thoughts and beliefs). Learning from experience and eventual change in self-concept (the physical, social, emotional and control /competence self-concept domains in this case) are hypothesised to be important determinants of long-term success. The power of relatedness (from self-determination theory) is acknowledged, but the need to ensure that change is embedded in social support within day-to-day life and not dependent on temporary relationships formed in intervention group settings is an important consideration. It is proposed that the processes of planning, self-regulation, making psychological changes and social interactions to address sources of tension and achieve long-term lifestyle change are teachable skills and techniques have been developed to facilitate this. The model provides a way of ensuring a clear focus on the challenge of long-term maintenance and will be used to the extent that it adds to or extends the above theories. Specifically, this includes the use of techniques to promote habit formation, to plan for sustainability (of social support relationships as well as behaviours), to address hedonistic needs, to address priority conflicts and to recognise and reinforce benefits in terms of self-concept change (particularly in the physical, emotional, social and competence domains).

2.2: Logic model

The logic model for REACT is shown in Figure 1. It identifies:

- The REACT intervention components and how they are delivered to participants

- The hypothesised mechanisms of action of the REACT intervention (causal assumptions about the process by which the intervention effects change in health behaviours and outcomes)
- The hypothesised contextual variables which might affect mechanisms of change in motivations and behaviour
- The hypothesised interaction between participation in the intervention, delivery quality, motivation, behaviour and outcomes.

The logic model also shows the types of data that will be collected for the process evaluation during the trial.

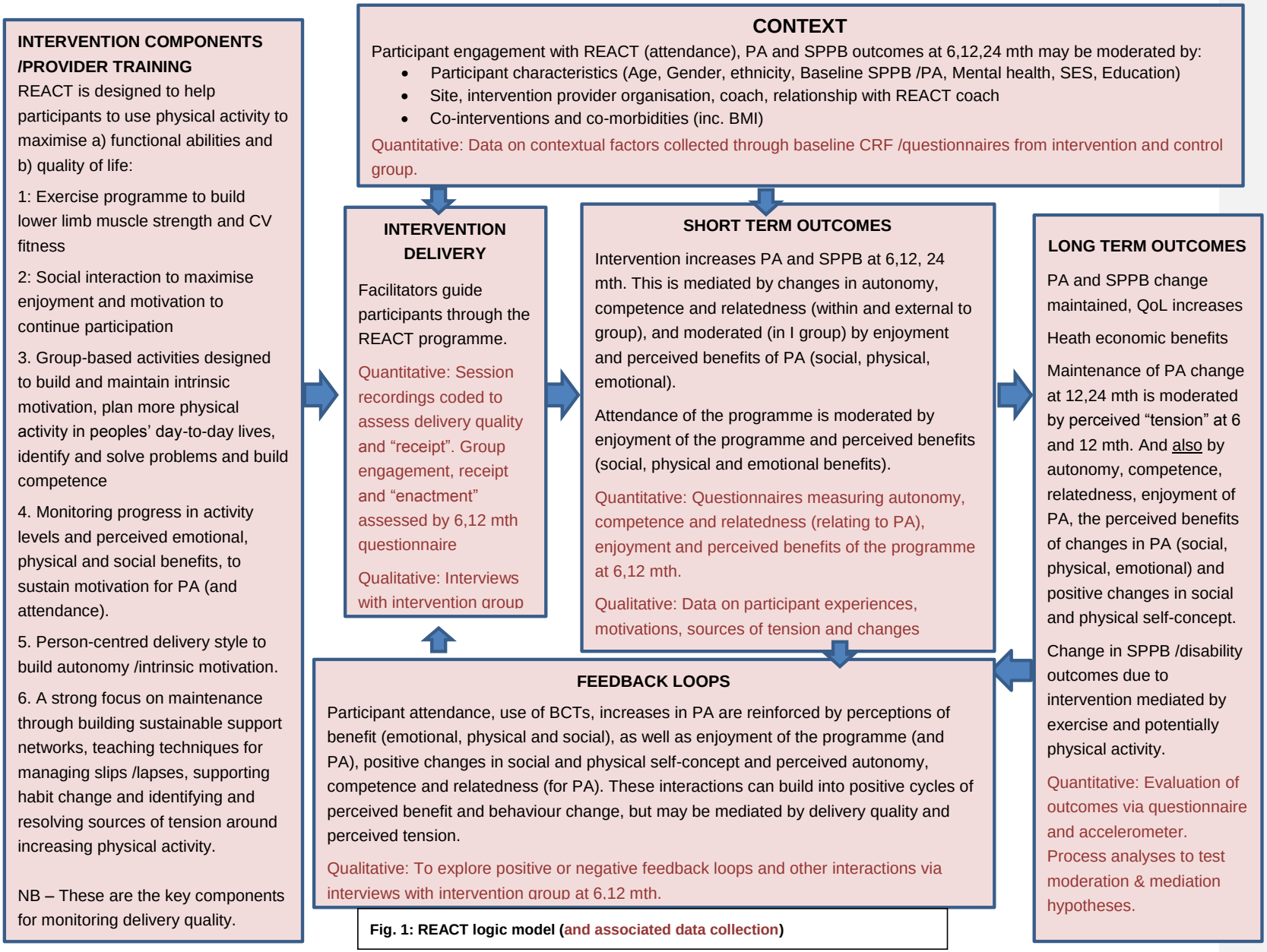
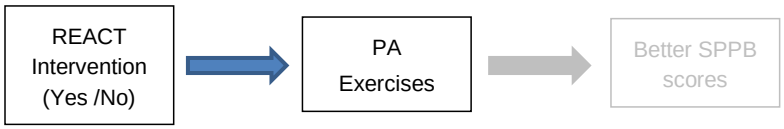


Fig. 1: REACT logic model (and associated data collection)

3. Hypotheses for process evaluation of the REACT intervention

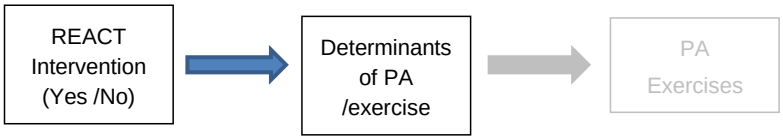
The hypotheses below are derived from the stated and implied assumptions in the above logic model and will be tested using process and outcomes data collected at baseline, 6 months (short term), 12 months (medium term) and 24 months (long term). The time from baseline to 12 months represents the intervention period (0-6 months = initial change and 6-12 months = supported maintenance) and the 12-24 month timeframe represents the post-intervention (unsupported maintenance) period.

Effects of the intervention on mediators of (and change in) lower limb physical function



1. Being in the intervention group will lead to changes in physical activity (MVPA, steps, sedentary time) and engagement in muscle-strengthening exercise from 0 to 6 months. This will be tested by comparison of change scores between intervention and control groups.
2. Increased exposure to the intervention (contact time) will correlate with increased change in physical activity (MVPA, steps, sedentary time) and engagement in muscle-strengthening exercise from 0-6 months. This will be tested by within group analyses.
3. Increased exposure to the intervention (contact time) will correlate with increased change in physical activity (MVPA, steps, sedentary time), engagement in muscle-strengthening exercise and SPPB score from 0-12 months. This will be tested by within group analyses.
4. Increased exposure to the intervention will lead to increased maintenance of physical activity and engagement in exercise. So, within the intervention group, intervention dose (contact time) will correlate negatively with decreases in PA, engagement in muscle-strengthening exercise and SPPB score from 6-12 months (during the supported maintenance period) and from 12-24 months (the unsupported maintenance period). This will be tested by within group analyses.

Effects of the intervention on mediators of PA and exercise



5. Exposure to the intervention will lead to changes in key psychosocial determinants of physical activity and exercise from baseline to 6 and 12 months.
    a. Compared with controls, the intervention group will experience increases in autonomy, competence (self-efficacy), relatedness, perceived intrinsic benefits of PA and exercise (social, physical and emotional) and enjoyment of PA and exercise from 0-6 months.
    b. Compared with controls, the intervention group will experience increases in physical activity-related self-concept, autonomy, competence (self-efficacy), relatedness, perceived intrinsic benefits of PA and exercise (social, physical and emotional) and enjoyment of PA and exercise from 0-12 months.
    c. Increased exposure to the intervention (total contact time from baseline to the relevant time point) will correlate with increased change in the above determinants (and in the expected direction).

Mediation and moderation of intervention effects on lower limb physical function

6. The intervention effect on SPPB (I vs C) may be mediated by changes in muscle-strengthening exercise, changes in balance and co-ordination exercise and by changes in MVPA, changes in lower intensity PA, or walking activity (steps per week). The amount of variance in SPPB explained by the different types of activity /exercise will be of interest.
7. The intervention effect on PA and exercise and the mediation effect of PA on change in SPPB score from 0-6, 0-12, 0-24 months may be moderated by a number of potential moderating variables, including Age, Gender, Ethnicity, Baseline physical activity and SPPB, Co-interventions, Co-morbidities, BMI, Mental health, Socio-economic status, Education level.
8. The intervention effect on *maintenance* of SPPB score from 6-12 and 12-24 months may be moderated by a number of potential moderating variables, including Age, Gender, Ethnicity, Baseline physical activity and SPPB, Co-interventions, Co-morbidities, BMI, Mental health, Socio-economic status, Education level.

Mediation and moderation of intervention effects on physical activity and exercise

9. Intervention effects on PA and muscle-strengthening exercise at 6 and 12 months will be mediated by 0-6 mth changes in autonomy, competence and relatedness in relation to PA and exercise, enjoyment of PA and exercise and perceived intrinsic benefits of PA and exercise (social, physical and emotional).
10. For those who succeed in increasing PA and exercise at 6 months (defined as an increase of at least 30 mins MVPA), the amount of change in PA maintained from 6 to 12 months (supported maintenance) will be moderated by measures of autonomy, competence and relatedness for PA and exercise, enjoyment,

perceived intrinsic benefits of PA and exercise (social, physical and emotional) at 6 months (NB: the predictor here is absolute values at 6 mths, not change scores).

11. For those who succeed in increasing PA and exercise at 12 months (defined as an increase of at least 30 mins MVPA), the amount of change in PA maintained from 12 to 24 months (unsupported maintenance) will be moderated by measures of autonomy, competence and relatedness for PA and exercise, enjoyment of and perceived intrinsic benefits of physical activity and exercise (social, physical and emotional) at 12 months (NB: the predictor here is absolute values at 12 mths, not change scores), as well as by change in physical activity related self-concept from 0-12 months.
12. For those who succeed in increasing PA and exercise at 6 months (defined as an increase of at least 30 mins MVPA), the amount of change in PA from 6 to 12 months (supported maintenance) will be moderated by perceived "tension" (see SkiM theory description for definition) of making changes in PA and exercise at 6 months. This analysis may need to be controlled for amount of PA and exercise increase (0-6 mths) as more extreme changes in PA or exercise should induce higher tension.
13. For those who succeed in increasing PA and exercise at 12 months (defined as an increase of at least 30 mins MVPA), the amount of change in PA from 12 to 24 months (unsupported maintenance) will be moderated by perceived tension of making changes in PA and exercise and changes in physical activity related self-concept at 12 months. This analysis may need to be controlled for amount of PA and exercise increase (0-12 mths) as more extreme changes in PA or exercise should induce higher tension.
14. For those who succeed in increasing PA and exercise at 6 and 12 months, low tension participants will have increased enjoyment of PA and exercise and a more positive physical activity related self-concept than higher tension participants at 6, 12 and 24 months (cross-sectionally and potentially prospectively also).
15. The relationship between intervention exposure (group allocation, contact time) and changes in PA and exercise from 0-6, 0-12, 0-24, 6-12 and 12-24 months may be moderated by a number of potential moderating variables, including Age, Gender, Ethnicity, Baseline physical activity and SPPB, Co-interventions, Co-morbidities, BMI, Mental health, Socio-economic status, Education.
16. The relationship between intervention exposure (group allocation, contact time) and changes in the determinants in this section may be moderated by a number of potential moderating variables (Age, Gender, Ethnicity, Baseline physical activity and SPPB, Co-interventions, Co-morbidities, BMI, Mental health, Socio-economic status, Education).

Mediators and moderators of programme attendance

17. Within the intervention group, programme attendance (contact time, number of sessions attended) from 0-6 months will be associated with enjoyment of the programme, positive perceptions of the facilitators and perceived benefits of PA and exercise (social, emotional, physical) at 6 months (absolute value, rather than change score).
18. Within the intervention group, programme attendance (contact time, number of sessions attended) from 0-12 months will be associated with enjoyment of the programme and perceived benefits of PA and exercise (social, emotional, physical) at 6 months (absolute values, rather than change scores).

Mediators and moderators of people joining the ambassadors programme

19. Within the intervention group, engagement with the ambassador programme (Yes /No) at 12 months will be associated with enjoyment of the programme, positive perceptions of the facilitators, relatedness in relation to PA and exercise (combined) and perceived benefits of PA and exercise (social, emotional, physical) at 6 months, and change in physical activity related self-concept (particularly social self-concept) from 0-12 months.

Additional considerations: Delivery style (and other engagement processes) and intervention fidelity may also moderate the effectiveness of the intervention. However, these concepts cannot be measured at the individual level and will only be assessed (through researcher observation of sessions) for a sub-sample of intervention sessions. These hypotheses may also be explored qualitatively.

4. Quantitative process evaluation

4.1 Participants /sampling

We will apply analyses to the whole sample where data is available, unless otherwise stated (e.g. some hypotheses apply only within the intervention group).

4.2 Measures

The following will be measured using brief questionnaires to allow testing of the above hypotheses:-

- Session attendance
- Total contact time for each participant
- Muscle strength /balance (SPPB scores)
- Physical activity (accelerometry) - time doing MVPA in bouts of either 1 or 10 minutes, steps, sedentary time)
- Engagement in muscle-strength exercise
- Physical activity related self-concept
- Perceived tension of maintaining current PA
- Perceived tension of maintaining current levels of exercise
- Autonomy in relation to PA
- Competence for PA
- Relatedness for PA
- Enjoyment of PA
- Perceived intrinsic benefits of PA (social, physical and emotional)
- Autonomy for strength-building exercise
- Competence for strength-building exercise
- Relatedness for strength-building exercise
- Enjoyment of strength-building exercise
- Perceived intrinsic benefits of strength-building exercise (social, physical and emotional)
- Enjoyment of the REACT programme (I group only)
- Credibility /identification with the session facilitators (I group only)
- *Demographic variables:* Age, Gender, Ethnicity, School leaving age, Marital status, Housing type, Ownership/rental status, Caring responsibilities, Baseline physical activity and SPPB, Co-interventions (0.6.12.24), Co-morbidities, BMI, (0,6,12,24), Mental health, Multiple Deprivation Index (from postcode), Education level.

Visit type	Scr	Scr	FU	FU	FU
Visit code		SV1	F06	F12	F24
Visit number		1	2	3	4
Telephone call	1				
Activity/assessment Month	-0.5	0	6	12	24
Form Name					
Verbal consent	X				
Telephone screening (some elements of inclusion and exclusion criteria)	X				
Written informed consent		X			
Contact information update	X	X	X	X	X
Demographic, social, economic	X				
SPPB battery		X	X	X	X
Accelerometry		X	X	X	X
Height and weight (weight only at 12m)		X		X	X
MoCA – Montreal Cognitive Assessment		X	X	X	X
PASE questionnaire		X	X	X	X
Dynometer (hand grip strength)		X	X	X	X
Ageing Well profile (social well-being scale only used at Bath/Bristol site)		X		X	X
Health-related quality of life (EQ-5D, SF-36)		X	X	X	X
Sleep Condition Indicator		X	X	X	X
Pain (Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC)		X			X
Mobility assessment tool-short form (MAT-sf)		X	X	X	X
Cognitive function (UK Biobank Healthy Minds Questionnaire)		X	X	X	X
Medical history		X			
Falls Inventory		X	X	X	X
Health and Social Service Usage		X	X	X	X
(fMRI imaging substudy) MRI scan, detailed cognitive assessment and gait analysis		X	X	X	

Session attendance (Intervention group only)			X	X	
Total contact time for each participant			X	X	
Physical activity related self-concept		X	X	X	
Perceived tension of maintaining current PA			X	X	X
Perceived tension of maintaining current exercise			X	X	X
Autonomy in relation to PA		X	X	X	X
Competence for PA		X	X	X	X
Relatedness for PA		X	X	X	X
Enjoyment of PA		X	X	X	X
Perceived intrinsic benefits of PA (social, physical and emotional)		X	X	X	X
Autonomy for strength-building exercise		X	X	X	X
Competence for strength-building exercise		X	X	X	X
Relatedness for strength-building exercise		X	X	X	X
Enjoyment of strength-building exercise		X	X	X	X
Perceived intrinsic benefits of strength-building exercise (social, physical and emotional)		X	X	X	X
Enjoyment of the REACT programme (Intervention group)			X	X	
Credibility /identification with the session facilitators (Intervention group only)			X	X	
Qualitative Interviews			X	X	X
Focus groups				X	X

Table 1: Process measures taken at each time point

4.3 Analyses

A detailed process evaluation analysis will be specified in due course. However, the types of analysis needed are either implied by or mentioned alongside the hypotheses above.

5. Qualitative process evaluation

5.1 Research Questions

The qualitative process evaluation will address five overarching questions:

RQ1. Was the intervention delivered as planned? Variations in intervention delivery by exercise specialists, including feedback on REACT training and implementation challenges will be investigated and recorded, as will variability in the acceptance/ receipt of the intervention by participants.

RQ2. Do any observed variations in delivery explain effectiveness / ineffectiveness of the intervention on physical function outcomes? What were the factors associated with engagement with REACT sessions? What made participants adhere to or drop-out from the programme?

RQ3. Do theorised mechanisms explain any observed impact on physical function and physical activity? Theorised change mechanisms, including key human needs (autonomy-relatedness-competence) identified in the Self Determination Theory, and other psychological and behaviour change processes (see section 2) will be investigated as mediators of intervention effects on physical function and physical activity.

RQ4. What other factors are associated with variation in intervention effectiveness among intervention recipients? Factors to be explored will include differences in participant characteristics (e.g. context/circumstances, ethnicity, deprivation index, beliefs and cognitions), perception of social connectedness and bonding within (and external to) groups, engagement with partner organisations, involvement with other activities offered by the same provider.

RQ5. What were participants', facilitators' and provider organisations' experiences of the REACT Ambassadors programme? Variations in programme delivery by facilitators, and the activities engaged in by Ambassadors including perceived benefits or disbenefits and implementation challenges will be investigated and recorded.

RQ6. Why did REACT partners decide to continue (or not continue) delivering the REACT exercise programme after the completion of the 12 month intervention? In what ways did the REACT intervention help to support ongoing PA and exercise after the 12 months intervention period (i.e. between 12 and 24 months)

? How did Ambassadors contribute to the maintenance of REACT?

These questions will be addressed in four distinct studies, data from which will be analysed using both qualitative and quantitative methods that will, collectively, constitute the process evaluation.

5.2 Study 1 Tracking the Experiences of Participants throughout the study: Repeated interviews addressing RQs 2,3,4,5, 7

Participants: 20 participants (5 at each centre (Bath/Bristol/Exeter/Birmingham)).

Data collection: The initial *face-to-face meeting of participants with their exercise leader* (45-60 minutes) will, with permission, be audio recorded by the exercise leader. This will provide data about the participants' initial expectations and motivations for taking part in the programme. To minimise early learning effects, the first two participants to whom an exercise leader delivers the intervention will be excluded from this sample. From the third participant onwards, twenty participants will be purposively selected by members of the process evaluation team. These twenty participants will represent a range of age, ethnicity and functional status and will include men and women and participants at all three sites. Selection will be facilitated by review of baseline data as provided by CTU via the web-based database. Topic guides will be developed for the 6,12 and 24 month interviews. The interviews will be conducted by the PhD student and the research assistants at each site. Verbatim meeting and interview transcripts will be categorised and organised using computer software NVIVO.

The research team will, with permission, *interview* each of these 20 participants, preferably on their own, at 6 months after the baseline visit (i.e. after participants have completed the adoption phase and they have entered the maintenance phase of the intervention), 12 months (post-intervention) and 24 months (follow-up) after the baseline visit, and audio record these interviews. All recorded meetings and the three interviews will be recorded verbatim. The researchers will summarise the content of the interview at the end of the discussion and invite the participants to add anything else they would like to share. The interviewees will be asked if they would like a copy of the summarised findings. This will be sent through the postal system and the participants will be invited to add comments if they wish.

Analysis: For each participant, transcripts of one face to face meeting, and three interviews will be available for framework analysis. Feedback received on research processes from data collected during the pilot phase will be used to refine the research processes of the main trial if needed. The PhD student will listen to the audio recordings several times to familiarize themselves with the data. Using NVIVO computer software, sections of data related to the aims will be assigned a code that summarizes the content either descriptively or interpretively. Codes with common features will be grouped together in predefined themes or new, emerging themes, before finally being assigned to interpretive overarching themes. Data about self-reported behaviour from the interviews will be compared with quantitative data on physical activity, exercise and session attendance collected during the study. Other members of the team will conduct independent analyses of subsets of the data, and the qualitative team will meet regularly to discuss their coding. Detailed notes of these discussions will be kept to help refine the analyses and to capture additional questions that could be answered from the data. Research reflexive memo notes will be used to assure transparency and trustworthiness of the analysis.
Participants' observed and self-reported responses to the intervention and their link to overall use and perceived benefit, will be explored to identify interpersonal processes that shape effectiveness or ineffectiveness of the intervention. At 6

months, participants' engagement with, response to the adoption phase of REACT (the structured exercise programme and the social/educational sessions) will be characterised and differences between participants noted. At 12 and 24 months overall evaluation of the intervention and maintenance of attendance and active lifestyle will be assessed and linked to responses at 6-months. This will allow a qualitative description of participants' experiences, potential pathways and barriers to maintenance/involvement with other local initiatives. The analyses will be carried out by the PhD student and AS with input from CG and JW, and the synthesis carried out by all four members of the qualitative team (AS,CG, KF, JW).

5.3 Study 2 Investigation of Experiences of REACT exercise leaders and provider organisations addressing RQs 1,5.

Participants: Up to 15 exercise leaders (at least 3 from each site) and all provider organisations at each site will be purposively sampled based on site of delivery.

Data collection: Focus groups will be conducted at 12 months from the time of intervention commencement in a mutually convenient venue. Focus groups are expected to last between 60-90 minutes. Focus groups will be conducted using a semi-structured interview guide allowing and encouraging participants to express their views. The researcher leading the exercise leaders' and community providers' interviews will work closely with the researcher conducting the participant interviews and review the topic guide throughout the study so that the questions are informed by relevant emerging topics. The research will also be guided by answers from the exercise leaders and the community providers and by further probing asking such as "tell me more about?" or "tell me how that made you feel?" Other techniques to enhance the interview include reflecting back on what was said, using non-verbal communication to show that the researcher is actively listing, for example, nodding, sitting forward, use of silence etc. The researcher will summarise the content of the interview at the end of the discussion and invite the participants to add anything else they would like to share. The interviewees will be asked if they would like a copy of the summarised findings. This will be sent through the postal system and the participants will be invited to add comments if they wish. The interviews will be carried out by the PhD student and the research assistants.

The researcher will write field notes at the end of each interview detailing how the interview was performed; reflect on their own performance and influence on the interview; how interviewees responded to the questions and initial thoughts about the main points arising from the interview.

All provider organisations will be assigned a code to ensure they remain anonymous. All other interviewees will have already been assigned a code. All focus groups will be audio recorded with the participants' permission and the interviews will be stored on encrypted laptops and a secure data base at the University of Bath. In transcripts, all identifiable information will be removed. No participant will be identified in any publication. A thank you letter for participating will be sent to the participant after the interview and a summary of the findings will be provided in due course (if desired by the participant).

Analysis: The data from both the individual interviews and the focus groups audio-recordings will be transcribed verbatim either by an experienced transcriber/secretary or a specialist software. Data analyses will use similar methods as applied in study 1. The analysis will be conducted by the PhD student and the process evaluation research team.

5.4 Study 3 Investigation of Experiences of REACT Ambassadors addressing RQ5

Participants: Up to 30 REACT Ambassadors (up to 9 Ambassadors at each site) will be purposively sampled based on site of delivery.

Data collection: Three focus groups will be conducted at 24 months from the time of intervention commencement in a mutually convenient venue. Focus groups are expected to last between 60-90 minutes. Focus groups will be conducted using a semi-structured interview guide focusing on the suitability of the Ambassadors training, challenges in implementing the programme and level of success of the programme. The interviews will be carried out by the PhD student and the research assistants.

Analysis: The data from the focus groups audio-recordings will be transcribed verbatim either by an experienced transcriber/secretary or a specialist software. Data analyses will use similar methods as applied in study 1. The analysis will be conducted by the PhD student and the process evaluation research team.

6. Assessment of intervention and training fidelity

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Fidelity of intervention delivery will be optimised and assessed using a range of the strategies outlined by the NIH Behaviour Change Consortium to assess and reinforce intervention fidelity8. These include checks to ensure that session delivery is compliant to treatment protocol. To maximise and monitor trial fidelity we will: (i) Optimise the fidelity of training and of the intervention design by reviewing the training and intervention materials (KF, AS and CG) to ensure that all elements relate to the theoretical basis described in section 2 above (ii) recruit REACT trainers with appropriate skills and experience, (iii) develop an accessible, standardised intervention manual, (iv) implement standardised REACT 'trainer training', (v) train more REACT trainers than needed to accommodate illness or withdrawal, and (vi) monitor delivery fidelity via recording of one-to-one consultation meetings for 20 participants and a sample of 4 sessions per intervention provider-pair (i.e. a minimum of 20 sessions) and the application of a 'fidelity checklist'. This approach worked well in our NIHR-funded EARS study9 and our REACH-HF study10. We will also record session attendance (intervention adherence) and relate this to outcomes. Specifically:

6.1 Study 4 Fidelity checks addressing RQ1

Data collection: A fidelity checklist will be developed and piloted during the internal pilot study (April to September 2016). This will be applied to 4 sessions per intervention provider-pair (i.e. a minimum of 20 sessions) and 20 individual face-to-face session recordings. This will clarify how well intervention components were delivered and received by participants and may identify components that were less well delivered. It will also allow researchers to describe variability in fidelity of delivery across sites and facilitators. Variability in the acceptance/ receipt of the intervention by participants might also be indicated by a) intervention completion, number of sessions attended and c) Physical function and physical activity progress data.

Analysis: Intervention fidelity scoring and analysis will be carried out by the PhD student and CG. An MSc student will act as a third coder and independently score a subgroup of 30 session recordings to help establish inter-rater reliability. Descriptive data (means and 95% confidence intervals) will be reported representing fidelity of delivery on each item of the checklist. The data will be summarised by facilitator-pairing, by site and overall (across all 4 sites).

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INTERVIEW TOPIC GUIDES

Study 1 Tracking the Experiences of Participants throughout the study: Repeated interviews addressing RQs 2,3,4,5, 7

Preamble script (6 month interview)

Thank you very much for agreeing to speak to me about participating in the REACT study, we really appreciate your time.

Can I just check that you remember a researcher speaking to you on the phone to ask if you would like to take part in the project? After the researcher spoke to you, you said that you were happy to take part in the project, including being interviewed as part of the research we are carrying out. The reasons for this meeting is to find out why you wanted to take part in REACT and how things have been during the first six months of your involvement with this programme.

The interview will take around 45 minutes and will be recorded to ensure that we do not miss anything. When we start the interview I will ask you to give your name and today's date, so that we have a record of your agreement to take part. However we will not use your name in any of our reports. If we use any quotes from you we will not give your name but use a false name.

Before we begin do you have any questions about doing the interview?

OK so the recorder is now going on….

1. First, can you give me your full name please?

2. And todays date is…….

3. Are you willing to agree to be interviewed by me? Thank you.

I will now go into some questions about your interest in the REACT project.

4. What appealed to you about REACT?

   Prompt for:
   -GP invited them to take part
   -programme addressing their worries about limitations in mobility
   -the possibility of being involved in a group exercise with people of their own age living locally
   -being part of a research study
   -anticipated health benefits

5. What did you think about the Participant Information Sheet?

   Prompt for:
   - was anything good about it?
   -was anything off putting about it?

-whether it influenced their decision to want to take part

6. What did you think about the call from the researcher who phoned you about taking part in the study?

   Prompt for:
   -was anything good about it?
   -was anything off putting about it?
   -whether it influenced their decision to want to take part?

7. What did you hope to gain from being involved in REACT in the first six months?

   Prompt for:
   -expectations
   -goals
   -personal health gain

8. Other than any benefit for you personally, do you think that your involvement in the research project might be useful in other ways?

   Prompt for:
   -benefits to other people
   -altruistic value of being involved in research

9. How strongly did these other benefits influence your wish to be involved in the project?

10. Can you think of reasons that some people might not want to be involved in the REACT study?

    Prompt:
    check for perceptions of impact of:
    -did not think they would benefit from the study
    -clarity of information about the project
    -time required to exercise
    -time required to complete q'naires
    -commitments
    -interest in exercise
    -Transport issues

11. Were these problems that you faced?

12. So that we can learn from your experience, did you overcome them?

    Prompt for:
    -how they did this
    -how would they encourage others to overcome these problems?

Moving now to the specific experiences of the first 6 months I would like to ask you about your first face-to-face meeting with the REACT leader.

13. How useful that meeting was?
    Prompt for whether the meeting covered:
    - participants' current physical activity profile
    -functional limitations and impact on daily activities
    -barriers to exercise
    -readiness to change
    - activity preferences
    -transport availability/suitability of allocated venue
    -support from family/friends

14. How was the interaction with the REACT leader?
    Prompt for whether the leader:
    -was professional, warm, empathetic, thoughtful, motivational
    -made participant feel at ease, safe, and confident that the programme will be delivered by experts in the field
    -explained in detail the programme requirements and commitment, the nature of exercise and what is expected by participants

15. At the end of that first face-to-face session were you sure about what being a REACT participant entailed?
    Prompt for:
    Understanding of REACT programme structure, need to commit for two years in terms of assessment, the combination of exercise and social/educational sessions.

I would like now to discuss the experience of participating in the exercise sessions which were initially held twice a week.

16. How did you find those exercise sessions?
    Prompt for:
    - Exercise intensity, gradual progression, comfort of doing the exercise with ankle weights, the balance exercises, the walking component
    - Social elements of the session, opportunities to socialise and build a social network
    - Organisation of sessions, suitability of venue
    - Issues related to these sessions
    - Recommendations for the delivery of these sessions

17. After the first 8 weeks, you also got involved in one social/educational session per week. How did you find those sessions?
    Prompt for:
    -Content of sessions, level of interest, opportunities for building social network, practical information about other community programmes
    -Motivation to explore other community programmes either delivered by the REACT partner or other community organisations
    -Decision to get involved with other community programmes
    -burden of attendance in one more session per week
18. After the first 12 weeks, REACT continued with one exercise session every week and one social/education session. How did you find that?
    Prompt for:
    –preference for one or two sessions a week
    – impact on motivation
    – any involvement with other initiatives
    – any plans to attend other initiatives with REACT group members
    – perceived level of support by REACT leader/partner to seek other local community initiatives

19. Is there anything else that you like to say about your experience in the first 6 months of REACT?

Thank you very much for taking part in this interview, it's been very helpful to hear about your views of the study. I really appreciate the time that you have given me today.

We will contact you again at the end of the 12 month REACT programme. This will help us get a full picture of your experience being a REACT member. We will not be using your name in any of the reports that we write.

Thank them again for their time.

Preamble script (12 month interview)

Thank you very much for agreeing to speak to me about participating in the REACT study, we really appreciate your time.

The reasons for this meeting is to discuss your experience of being a REACT member for the last 12 months. Now that the programme has been completed is a great opportunity to get your feedback about what worked well and how we can improve the programme further.

The interview will take around 30 minutes and will be recorded to ensure that we do not miss anything. When we start the interview I will ask you to give your name and today's date, so that we have a record of your agreement to take part. However we will not use your name in any of our reports. If we use any quotes from you we will not give your name but use a false name.

Before we begin do you have any questions about doing the interview?

OK so the recorder is now going on….

20. First, can you give me your full name please?

21. And todays date is…….

22. Are you willing to agree to be interviewed by me? Thank you.

I will now go into some questions about your involvement in the REACT project.

23. How often did you attend the REACT sessions (retrieve their individual register so know in advance their session attendance rate)?

24. What made you continuing attending the REACT sessions for 12 months?

    Prompt for:
    -enjoyment, social interaction, social network
    -health benefits particularly evidence of functional improvements
    -interaction with session leaders
    -habit formation
    -social/educational sessions as a motive
    -interaction with delivery organisation
    -feelings of worth, respect
    -contribution to a research study
    -support by family members, friends, GP, other

25. What were reasons for not attending some sessions?
    Prompt for:
    -health reasons including hospitalisations
    -carer responsibilities (partners, grandchildren)

-weather
-being away on holiday
-other commitments

26. After the first 6 months, REACT continued with one exercise session every week and one social/education session every month. How did you find that?
    Prompt for:
    –content of sessions
    -interest, enjoyment
    -preference for more contact
    -impact on competence and confidence
    – impact on motivation to continue being active
    – perceived level of support by REACT leader/partner organisations to seek other local community initiatives

27. Since our last meeting have you joined any other initiatives?
    Prompt for:
    – any involvement with other initiatives
    – any plans to attend other initiatives with REACT group members

28. What did you hope to gain from being involved in REACT in the first 12 months?

    Prompt for:
    -expectations
    -goals
    -personal health gain

29. Can you think of reasons that some people might not have attended many REACT sessions?

    Prompt:
    -did not see improvements in functional ability
    -not interesting/enjoyable
    -did not maintain the social connectedness with other REACT members
    -time required to exercise
    -commitments
    -interest in the specific exercise programme

-Transport issues

30. Could you think of ways to improve the programme?

    Prompt for:
    -inclusion of other exercise types
    -Enhancement of social/fun elements
    -signposting and support to attend other initiatives

    Now focussing in the next 12 months I would like to ask you:

31. How confident you feel you will continue being active?
    Prompt for:
    - ruler of confidence “from zero meaning not confident at all, to 10 meaning very confident”. Why did participants score a certain number? How could they improve that score?
    -facilitators and barriers to activity
    - ruler of importance “from zero meaning not important at all, to 10 meaning very important”. Why did participants score a certain number? How could they improve that score?
    -functional limitations and impact on daily activities
    - activity preferences
    -transport availability/suitability of allocated venue
    -support from family/friends/REACT ambassadors

32. If REACT sessions were available for one more year but a small fee of attendance would you be interested to continue participating?

33. Is there anything else that you like to say about your experience in the first 12 months of REACT?

Thank you very much for taking part in this interview, it’s been very helpful to hear about your views of the study. I really appreciate the time that you have given me today.

We will contact you again at the end of the 24 month REACT programme. This will help us get a full picture of your experience being a REACT member. We will not be using your name in any of the reports that we write.

Thank them again for their time.

Preamble script (24 month interview)

Thank you very much for agreeing to speak to me about participating in the REACT study, we really appreciate your time.

The reasons for this meeting is to discuss how things have been for you the year after the REACT exercise programme was completed. Remember, the aim of REACT was to support people to maintain an active lifestyle. A year later, it is now a great opportunity to get your feedback about how things have been for you.

The interview will take around 20 minutes and will be recorded to ensure that we do not miss anything. When we start the interview I will ask you to give your name and today's date, so that we have a record of your agreement to take part. However we will not use your name in any of our reports. If we use any quotes from you we will not give your name but use a false name.

Before we begin do you have any questions about doing the interview?

OK so the recorder is now going on….

34. First, can you give me your full name please?

35. And todays date is…….

36. Are you willing to agree to be interviewed by me? Thank you.

I will now go into some questions about your involvement in community initiatives.

37. Did you attend other exercise specific sessions? If yes, then prompt:
    What type of sessions? How often? Did you attend sessions provided by the REACT partner or sessions provided by other community providers?

    If no, then prompt:

    What were the reasons for not attending other exercise sessions? Explore barriers including motivational, personal, social, environmental barriers.

38. Did you attend other community initiatives? If yes, then prompt:
    What type of initiatives? How often? Did you attend initiatives provided by the REACT partner or initiatives provided by other community providers?

    If no, then prompt:

    What were the reasons for not attending other community initiatives? Explore barriers including motivational, personal, social, environmental barriers.

39. Did you get any support by our REACT Ambassadors? If yes, then prompt:
    -What was that support? Was it useful?
    If no, then explore reasons that they did not interact with REACT Ambassadors.

40. Did you get any support by community resources such as health visitors, health friends schemes, etc.? If yes, explore how useful that was?

41. Did you keep contact with your REACT group members? If yes, how often do you meet? Do you organise days out/meeting for meals or coffee/going to cinema or other activities?

42. Thinking of the last two years of your involvement with the REACT study what:

    A. Were the things you enjoyed most?
    B. Were the things you least enjoyed/did not like?

43. Looking back at the reasons for joining REACT, did you gain the things you expected by being involved in REACT?

    Prompt for:
    -expectations
    -goals
    -personal health gain

    If not, why do you think your expectations were not met?

44. How could we improve REACT to support people to maintain an active lifestyle in a more effective way in the future?
    -Transport issues

Thank you very much for taking part in this interview and for all your support and input during the REACT study. Your information is invaluable. I really appreciate the time that you have given me today and in our previous discussions.

I would like to wish you all the best. You will get more REACT newsletters with information about the outcomes of the study. We will not be using your name in any of the reports that we write.

Thank them again for their time.

5.3 Study 2 Investigation of Experiences of REACT exercise leaders addressing RQs 1,5.

Preamble script (12 month interview)

Thank you very much for agreeing to speak to me about participating in the REACT study, we really appreciate your time. As a REACT exercise leader you have played an important role in the implementation of the REACT programmerogramme. Our next step is to gain a deeper understanding of your REACT experience. This will enable us to evaluate the acceptability of the programme and ways to further improve it.

The interview will take around 30 minutes and will be recorded to ensure that we do not miss anything. When we start the interview I will ask you to give your name and today's date, so that we have a record of your agreement to take part. However we will not use your name in any of our reports. If we use any quotes from you we will not give your name but use a false name. During the interview please speak clearly and remember there are no right or wrong answers, we simply want to hear your opinions.

Before we begin do you have any questions about doing the interview?

OK so the recorder is now going on….

45. First, can you give me your full name please?

46. And todays date is…….

47. Are you willing to agree to be interviewed by me? Thank you.

1. *Going right back to the beginning of REACT why did you decide to apply to be a REACT exercise leader?*
2. *What did you think about the REACT training sessions?* Do you think the training was sufficient? *Was there anything that could have been improved?*
3. *How did you find working with the REACT participants? Was there anything you would have changed / any challenges you faced?*

Moving now to the specific experiences of the REACT intervention I would like to ask you about your first face-to-face meeting with the REACT participant:

How useful that meeting was?

Prompt for whether the meeting covered:
- participants' current physical activity profile
-functional limitations and impact on daily activities
-barriers to exercise
-readiness to change
- activity preferences
-transport availability/suitability of allocated venue

-support from family/friends

I would like now to discuss the experience of delivering the exercise sessions which were initially held twice a week.

48. How did you find the structure and the content of those exercise sessions?

Prompt for:

- *Exercise intensity, gradual progression, comfort of doing the exercise with ankle weights, the balance exercises, the walking component*
- *Social elements of the session, opportunities to socialise and build a social network*
- *Organisation of sessions, suitability of venue*
- *Issues related to these sessions*
- *Recommendations for the delivery of these sessions*

49. After the first 8 weeks, you also delivered one social/educational session per week. How did you find those sessions?

Prompt for:

-Content of sessions, level of interest, opportunities for building social network, practical information about other community programmes

-Motivation to explore other community programmes either delivered by the REACT partner or other community organisations

-burden for participants attending one more session per week

50. After the first 12 weeks, REACT continued with one exercise session every week and one social/education session. How did you find that?

Prompt for:

–preference for one or two sessions a week

– impact on participants' motivation

– supporting REACT participants to make plans and attend other initiatives

51. How did you go about identifying local Physical Activity programme and other initiatives? Prompt:

-Was it easy to identify local Physical Activity opportunities?

-Were the provider organisations receptive to you and the REACT programme?

-What different methods did you use to identify these opportunities?

-Do you think REACT participants could have done this without your help?

52. *Your main role was to support the REACT participants to gradually improve their physical function and increase their physical activity. How do you think that worked? Is there anything that you think could have been improved in terms of the support we offered to the REACT participants?*

53. How do you think being involved in REACT impacted the Ambassadors and Participants' lives? *Separate questions*

54. Do you consider REACT as a useful model to *help* older people with functional limitations become more active and engage and connect socially with their communities? *Why?*

55. What would you say the strengths and weaknesses of the REACT intervention were?

5.3 Study 2 Investigation of Experiences of REACT provider organisations addressing RQs 1,3,4,5,6

Preamble script (24 month interview)

Thank you very much for agreeing to speak to me about being a provider of the REACT programme, we really appreciate your time. As a REACT provider you have played an important role in the implementation of the REACT programme. Our next step is to gain a deeper understanding of your REACT experience. This will enable us to evaluate the acceptability of the programme and ways to further support provider organisations which would like to deliver REACT in the future.

The interview will take around 30 minutes and will be recorded to ensure that we do not miss anything. When we start the interview I will ask you to give your name and today's date, so that we have a record of your agreement to take part. However we will not use your name in any of our reports. If we use any quotes from you we will not give your name but use a false name. During the interview please speak clearly and remember there are no right or wrong answers, we simply want to hear your opinions.

Before we begin do you have any questions about doing the interview?

OK so the recorder is now going on….

56. First, can you give me your full name please?

57. And todays date is…….

58. Are you willing to agree to be interviewed by me? Thank you.

59. Going right back to the beginning of REACT why did you decide to support REACT by providing in-kind or financial support for the intervention delivery?

60. What did you think about the REACT exercise leader training sessions? Do you think the training was sufficient? Was there anything that could have been improved?

61. How did you find the structure of the REACT sessions? Was there anything you would have changed / any challenges you faced?

62. How did you find the Ambassadors' programme? Was there anything you would have changed / any challenges you faced?

63. Do you consider that REACT is a useful model to support older people to improve their physical function and physical activity levels?
64. What would you say are the strengths and weaknesses of the REACT intervention?
65. Did you deliver REACT beyond the first 12 months? What were the reasons for your decision of continuing or not continuing offering the REACT sessions during the following 12 months?
66. How does REACT compare to similar programmes you are involved with/manage?
67. What challenges *did you face* whilst delivering the REACT intervention?

5.4 Study 3 Investigation of Experiences of REACT Ambassadors addressing RQ5

Preamble script (12 and 24 month interview)

Thank you very much for agreeing to speak to me about being an Ambassador of the REACT programme, we really appreciate your time. As a REACT Ambassador you have played an important role in the implementation and maintenance of the REACT programme. Our next step is to gain a deeper understanding of your REACT Ambassador experience. This will enable us to evaluate the acceptability of this new programme and ways to further support REACT participants who would like to become Ambassadors in the future.

The interview will take around 30 minutes and will be recorded to ensure that we do not miss anything. When we start the interview I will ask you to give your name and today's date, so that we have a record of your agreement to take part. However we will not use your name in any of our reports. If we use any quotes from you we will not give your name but use a false name. During the interview please speak clearly and remember there are no right or wrong answers, we simply want to hear your opinions.

Before we begin do you have any questions about doing the interview?

OK so the recorder is now going on….

68. First, can you give me your full name please?

69. And todays date is…….

70. Are you willing to agree to be interviewed by me? Thank you.

(12 months only)

71. Going right back to the beginning of the Ambassadors' programme why did you decide to become an Ambassador?

72. What did you think about the two Ambassador training options? Which one did you choose and why?
73. Which skills did you bring to the role? Which skills do you think you developed during the Ambassadors' training programme?
74. Do you think the Ambassadors' training was sufficient? Was there anything that could have been improved?

75. How did you find the structure of the Ambassadors programme sessions? Was there anything you would have changed

76. Did you face any challenges in preparing for your Ambassadors' role? How did you overcome them?

77. What challenges *did you face* whilst being an Ambassador for REACT?

(12 and 24 months)

78. Do you consider that the Ambassadors' programme is a useful model to support older people to improve their physical function and increase and maintain their physical activity levels?

79. What would you say are the strengths and weaknesses of the REACT Ambassadors' programme?

80. Could you think of ways to improve the Ambassadors' programme?

81. What would you describe as successes and challenges of being a REACT Ambassador?

(24 months only)

82. Did you deliver the Ambassadors' programme beyond the first 12 months? What were the reasons for your decision of continuing or not continuing acting as an Ambassador during the following 12 months?

83. Now that REACT has ended, do you consider of continuing being an Ambassador for the REACT provider organisation or other providers in your community?

Appendix 11 University of Birmingham report of serious adverse event form

Serious Adverse Event Form

E-mail: researchgovernance@contacts.bham.ac.uk

A serious adverse event (SAE) is any medical occurrence that results in death, is life-threatening, requires or prolongs unplanned hospitalisation, causes persistent or significant disability, results in congenital abnormalities or represents potentially serious harm to research patients and others.

Please complete this form using black ink and BLOCK capitals. Options should be selected by placing a cross (X) in the appropriate box.

Once complete please scan and send electronically to the above email [University of Birmingham] as soon as possible, ideally within 24 hours, of the event taking place. If you have any questions related to this form or reporting please ring the Research Governance Office on: 0121 4147618.

Study Details

Study Name	REACT (RETIREMENT I ACTION)	**MREC:**	**15/LO/2082**
ISCRTN:	**45627165**	**UKCRN:**	**20578**

Details of Chief Investigator (CI)

Name	AFRODITI STATHI
Address	UNIVERSITY OF BIRMINGHAM, EDGBASTON, BIRMINGHAM B15 2TT
Telephone	0121 415 8389
Email	A.STATHI@BHAM.AC.UK

Section 1 – Participant & Site Details

1. **Study Name:** **REACT**
2. **Patient ID:**
3. **Patient Initials:**
4. **Date of Birth:**

D D M M Y Y Y Y

5. **Site Name:**

Section 2 – Serious Adverse Event (SAE) Details

5. SAE Onset Date: ☐☐ ☐☐ ☐☐☐☐ (D D M M Y Y Y Y)

6. Seriousness Criteria (check all that apply):

- ☐ Resulted in Death
- ☐ Life Threatening
- ☐ Persistent / Significant Disability / Incapacity
- ☐ Congenital anomaly / Birth defect
- ☐ Hospitalisation / Prolongation of Hospitalisation
- ☐ Other medically important condition

Admission date ☐☐ ☐☐ ☐☐☐☐ (D D M M Y Y Y Y)

Discharge date ☐☐ ☐☐ ☐☐☐☐ (D D M M Y Y Y Y)

7. Relationship to research procedures:

☐ None ☐ Possible ☐ Probable ☐ Definite

If related to Research Procedures (possibly, probably or definitely), expectedness:

☐ Expected ☐ Unexpected

8. Severity: ☐ Mild ☐ Moderate ☐ Severe

9. Outcome: ☐ Recovered ☐ Recovered with sequelae ☐ Recovering ☐ Not Recovered ☐ Unknown ☐ Fatal

Date of recovery ☐☐ ☐☐ ☐☐☐☐ (D D M M Y Y Y Y)

Section 3 – Serious Adverse Event Narrative

10. Please provide a description of the SAE and follow-up infomration as required:

Include presenting signs and symptoms, course of events, treatments for the event and outcomes. Continue on separate sheet if necessary and attach relevant medical notes (remembering to sign and date).

11. Has the event resolved: ☐ **Yes** ☐ **No** ☐ **On going**

12. Date resolved: ☐☐ ☐☐ ☐☐☐☐ (D D M M Y Y Y Y)

Section 4 – Form Details

13. Type of report: ☐ **Initial** ☐ **Follow-up**

13. Date SAE form completed: ☐☐ ☐☐ ☐☐☐☐ (D D M M Y Y Y Y)

14. Signature of reporting person:

16. Please Print Name:

17. Please Print Position:

For [University] use ONLY

1. Date received: ☐☐ ☐☐ ☐☐☐☐ (D D M M Y Y Y Y)

2. Date entered on database: ☐☐ ☐☐ ☐☐☐☐ (D D M M Y Y Y Y) **3. Entered by:** ☐☐

4. Name of reviewer:
(CI or Medical Monitor)

5. Date of review: ☐☐ ☐☐ ☐☐☐☐

6. Type of event: SAE ☐ SAR ☐ SUSAR ☐

7. Further action required: NO ☐ YES ☐

8. Comments:

Reviewer, Signature: **Date:**

CI, Signature: **Date:**

Section 5 – Acknowledgement of receipt by main REC (South West – Frenchay)

The [ ] Research Ethics Committee acknowledges receipt of the above.

Signed:	
Name:	
Position on REC:	
Date:	

Signed original to be sent back to Chief Investigator (or other person submitting report).

Appendix 12 Guidance for potentially serious breaches of GCP

Commented [JW1]: Do we need a Birmingham version – or just change Bath to Birmingham

Guidance for reporting potential serious breaches of good clinical practice / trial protocol in clinical research sponsored by the University of Bath

Contents

1. Purpose and Objective

1.1. Definition and Scope[1]

A Serious Breach of Good Clinical Practice (CGP) or Trial Protocol is defined as a breach which is likely to effect to a significant degree i) the safety or physical or mental integrity of the subjects of the trial or ii) the scientific value of the trial.

1.2. Potential serious breaches of Good Clinical Practice (CGP) or Trial Protocol

The purpose of this document is to identify and standardise the process for reporting Serious Breaches of GCP or of the Trial Protocol. Regulation 29A of the Medicines for Human Use (Clinical Trials) Regulations 2004 [Statutory Instrument 2004/1031], as amended by Statutory Instrument 2006/1928, contains a requirement for the notification of 'serious breaches 'of GCP or the trial protocol, by the sponsor to the MHRA within 7 days of becoming aware of that breach. Although the sponsor has delegated the responsibility of identifying and assessing serious breaches occurring during the day to day running of a clinical trial to the PI, the sponsor will be responsible for notifying the MHRA of the serious breach.

2. Responsible personnel and procedure

In respect of potential breaches of GCP or the trial protocol, the responsibilities are as follows:

[1] To report any potential cases of **misconduct or fraud** in projects sponsored by the University of Birmingham, please refer to the University's Research misconduct policy, available from https://www.birmingham.ac.uk/Documents/university/legal/15-16/code-of-practice-research.pdf

	Responsibility	Activity
1.	Principal Investigator/ Research team	A serious breach of GCP or the trial protocol is defined as a breach which is likely to effect to a ***significant*** degree i) The safety or physical or mental integrity of the subjects of the trial or ii) The scientific value of the trial
2.	Principal Investigator/Research team	If a breach of GCP or protocol occurs during a trial, this may be identified through routine monitoring, internal audits or during the day to day running of the trial. The PI needs to be notified of the breach as soon as possible by the monitor, auditor or study team. The PI for the study needs to make an assessment of the severity of the breach. If the breach is classified by the PI as a 'serious breach' according to the definition above and if the University of Birmingham is the sponsor, the PI should complete a 'Notification of Serious Breach of GCP or Trial Protocol Form' (Appendix A).
3.	Principal Investigator/ Research Team	The notification form has to be signed by the PI or other medically qualified person who is fully aware of the trial protocol, and authorised to do so by the PI.
4.	Principal Investigator /Research Team	The PI should scan and email the notification form over to the Vice Chancellor's Office within **24hrs** of becoming aware of the breach (email: m.wells@bath.ac.uk).
5.	Principal Investigator/Research Team	Deviations from clinical trial protocols and GCP occur commonly in clinical trials. The majority of these instances are technical deviations that do not result in harm to the trial subjects or significantly affect the scientific value of the reported results of the trial. These cases should be documented e.g. in the case report form for the trial or trial master file in order for appropriate corrective and preventative actions to be taken. In addition, these deviations should be included and considered when the clinical study report is produced, as they may have an impact on the analysis of data. However, not every deviation from the protocol needs to be reported as a 'serious breach'. Please refer to (Appendix B) for further guidance on the notification of Serious Breaches of GCP or the Trial Protocol.
6.	Sponsor	Once the PI has notified the sponsor of a serious breach or has completed the 'Notification of Serious Breach of GCP or Trial Protocol Form' (Appendix A) Send the notification of serious breach form to GCP-PV.Inspectors@mhra.gsi.gov.uk OR GCP Inspectorate, MHRA, 18-103, Market Towers, 1 Nine Elms Lane, London, SW8 5NQ within **7 days** of becoming aware of the breach.

APPENDIX A

UNIVERSITY OF BATH NOTIFICATION FORM OF POTENTIAL BREACHES OF GOOD CLINICAL PROTOCOLR THE TRIAL PROTOCOL IN CLINICAL RESEARCH SPONSORED BY THE UNIVERSITY OF BATH

Title of trial:	
Chief Investigator's name:	
Name of sponsor:	
Study site where the issue(s) occurred: (UK site)	
Was this a potential breach of GCP or the Trial Protocol:	
Name and Contact Details of person reporting reaction:	
Date the incident(s) occurred:	
Date incident(s) reported to trial staff:	
Details of the incident(s) (please specify if it is a patient safety/data integrity issue or both, or something else)	

(Continue on separate sheets if required) Details of any action taken by trial staff:	

CI/PI's name	Signature:
Date:	

For Vice-Chancellor's Office use only

Date report received: Received By:	
Date MHRA notified: Notified By:	

APPENDIX B

GUIDANCE FOR THE NOTIFICATION OF SERIOUS BREACHES OF GCP OR THE TRIAL PROTOCOL

Table of Contents

A. Legal requirement:

Regulation 29A of the Medicines for Human Use (Clinical Trials) Regulations 2004 [Statutory Instrument 2004/1031], as amended by Statutory Instrument 2006/1928, contains a requirement for the notification of “serious breaches” of GCP or the trial protocol:

“29A. (1) The sponsor of a clinical trial shall notify the licensing authority in writing of any serious breach of -

(a) the conditions and principles of GCP in connection with that trial; or

(b) the protocol relating to that trial, as amended from time to time in accordance with regulations 22 to 25, within 7 days of becoming aware of that breach.

(2) For the purposes of this regulation, a “serious breach” is a breach which is likely to effect to a significant degree –

(a) The safety or physical or mental integrity of the subjects of the trial; or

(b) The scientific value of the trial”.

B. Purpose of the requirement:

The new requirement was implemented in UK legislation in order to:

1. Enhance the safety of trial subjects/patients by seeking to ensure that the licensing authority is promptly informed of such serious breaches, in order to take appropriate action in response to the breach and/or,

2. To take the information regarding serious breaches into account when assessing future applications for clinical trial authorisation, and applications for marketing authorisation, which include data from trials affected by serious breaches.

C. Purpose of this guidance:

- To outline the practical arrangements for notification.
- To provide advice on what should and what should not be classified as a "serious breach" and what must be reported.
- To outline possible actions that may be taken by the MHRA in response to notifications of serious breaches.

D. Arrangements for notification:

Who should notify?

The Sponsor or a person legally authorised by the Sponsor to perform this function (e.g. legal representative or contract research organisation), if this function has been delegated by the Sponsor to another party. In accordance with Statutory Instrument 2004/1031 as amended by Statutory Instrument 2006/1928, the Sponsor retains legal responsibility even if the function is delegated (Regulation 3.12). The CRO is also legally responsible for compliance with the legislation in relation to functions delegated by the Sponsor to the CRO (Regulation 3.8).

When should the notification be made?

- Within 7 days of the Sponsor becoming aware of the breach. If the notification function has been delegated by the Sponsor to another party e.g. a CRO, the 7-day timeline applies to the other party.

- If the Sponsor retains the notification function, then it is recommended that agreements between the Sponsor and other parties involved in the trial e.g. CROs, contractors, co-development partners, investigators, should state that the other party will promptly notify the Sponsor of a serious breach (as defined in Regulation 29A) that they become aware of, in order for the Sponsor to meet their legal obligation. In this case, the clock starts when the Sponsor becomes aware of the serious breach.

- If the Sponsor obtains clear and unequivocal evidence that a serious breach has occurred (as defined in Regulations 29A), the default position should be for the Sponsor to notify the MHRA first, within 7 days, and investigate and take action simultaneously or after notification. In this case, the Sponsor should not wait to obtain all of the details of the

breach prior to notification. In other cases, some degree of investigation and assessment may be required by the Sponsor prior to notification, in order to confirm that a serious breach has actually occurred.

- A pragmatic approach to clock start should be employed. Inspectors will review the process for notification during MHRA GCP inspections and delays in notification may be classified as a non-compliance. If in doubt about whether and when to notify, contact the MHRA GCP Inspectorate.

Who should be notified?

- Notify serious breaches to the MHRA GCP Inspectorate. Notifications should primarily be made using the following email address:

  E-mail to: GCP-PV.Inspectors@mhra.gsi.gov.uk

- A template form for notifications of serious breaches to the MHRA is attached in Appendix II.

- The Sponsor may initially contact the MHRA Inspectorate by telephone to discuss the breach and follow up with a written notification within 7 days of the Sponsor becoming aware of the breach. For current contact details for the Inspectorate, please refer to the MHRA web site.

- Notifications can also be sent by post or fax to any of the three MHRA Inspectorate offices. Current office addresses can be found on the MHRA web site.

- Wherever possible, MHRA will provide an acknowledgement of receipt of notifications. If the MHRA template form is not used, the written report should clearly state that it relates to a notification of a serious breach.

E. Identifying serious breaches:

Deviations from clinical trial protocols and GCP occur commonly in clinical trials. The majority of these instances are technical deviations that do not result in harm to the trial subjects or significantly affect the scientific value of the reported results of the trial. These cases should be documented e.g. in the case report form for the trial or trial master file, in order for appropriate corrective and preventative actions to be taken. In addition, these deviations should be included and considered when the clinical study report is produced, as they may have an impact on the analysis of the data. However, not every deviation from the protocol needs to be reported to the MHRA as a serious breach.

What needs to be reported?

- Any serious breach of:

  (a) the conditions and principles of good clinical practice in connection with that trial *(as defined in UK legislation)*; or

  (b) the protocol relating to that trial, as amended from time to time in accordance with regulations 22 to 25.

- For the purposes of this regulation, a "serious breach" is a breach which is likely to effect to a significant degree:

(a) the safety or physical or mental integrity of the subjects of the trial *(this should be relevant to trial subjects in the UK)*; or

(b) the scientific value of the trial.

The judgement on whether a breach is likely to have a significant impact on the scientific value of the trial depends on a variety of factors e.g. the design of the trial, the type and extent of the data affected by the breach, the overall contribution of the data to key analysis parameters, the impact of excluding the data from the analysis etc.

It is the responsibility of the Sponsor to assess the impact of the breach on the scientific value of the trial.

This assessment should be documented and the appropriateness of the decisions taken by the Sponsor may be examined during MHRA inspections. If the Sponsor is unclear about the potential for a breach to have significant impact on the scientific value of the trial, the Sponsor should contact the MHRA to discuss the issue.

Examples illustrating breaches classified as serious or non-serious (this is not an exhaustive list):

1. A breach of GCP or the protocol leading to the death, hospitalisation or permanent disability of a trial subject in the UK. Please note, not every serious adverse event (SAE) or suspected unexpected serious adverse reaction (SUSAR) would routinely be classified as a serious breach, but SAEs/SUSARs resulting from a breach of the conditions and principles of GCP or a breach of the protocol may constitute a serious breach. Submission of a serious breach notification to the MHRA Inspectorate does not obviate the requirement for a SUSAR report, where applicable, to be submitted to the concerned competent authorities e.g. via the EudraVigilance database.

2. Proof of fraud relating to clinical trial records or data, if the fraud is likely to have a significant impact on the integrity of trial subjects or the scientific value of the data.

   Although not a legal requirement under 29A, the MHRA GCP Inspectorate encourages the reporting of all confirmed instances of clinical trial fraud occurring at sites in the UK, which the Sponsor becomes aware of. The reason for this is that, although fraud at one particular trial site may not have a significant impact on scientific value or subject integrity for that particular trial, the MHRA would wish to assess the impact on other trials or subjects/patients at that site.

   If clinical trial fraud is identified at a non-UK trial site, for a trial that is also being conducted in the UK, a serious breach notification should be submitted to MHRA if the fraud is likely to have a significant impact on the integrity of trial subjects in the UK or on the overall scientific value of the trial. A site refers to any site involved in the trial e.g. CRO or other contracted organisation and not solely to investigator sites.

3. Persistent or systematic non-compliance with GCP or the protocol that has a significant impact on the integrity of trial subjects in the UK or on the scientific value of the trial. For example, widespread and uncontrolled use of protocol waivers affecting eligibility criteria, which leads to harm to trial subjects in the UK or which has a significant impact on the scientific value of the trial. Another example would be of an investigator repeatedly failing to reduce or stop the dose of an IMP in response to a trigger (e.g. abnormal laboratory results) defined in the protocol.

4. Failure to control investigational medicinal product(s) such that trial subjects or the public in the UK are put at significant risk or the scientific value of the trial is compromised. If a serious breach occurs due to an IMP defect, a drug defect report may need to be submitted to the MHRA Defective Medicines Reporting Centre (DMRC), in addition to the serious breach notification.

5. Failure to report adverse events, serious adverse events or SUSARs in accordance with the legislation, such that trial subjects, or the public, in the UK are put at significant risk e.g. inadequate safety reporting in dose escalation studies may have an impact on the decision to escalate to the next dose level.

6. For trials that are on-going in the UK, should serious breaches that occur at non-UK sites be reported?

   Example:

   a. A serious breach is identified at an investigator site in Mexico. The breach has a significant impact on the integrity of trial subjects at the Mexican site and is likely to have a significant impact on the integrity of trial subjects in the UK. For example, the cause of the breach is such that the breach may occur at other trial sites, e.g. death of a subject due to incorrect administration of IMP resulting from erroneous reconstitution instructions in the protocol. Notify the MHRA of the serious breach (other concerned competent authorities may also need to be informed).

      In relation to the example quoted, an urgent safety measure (USM) may need to be implemented to address the cause of the breach. If, in order to address the cause of a serious breach, a USM is implemented at UK sites, to amend the conduct of the trial or suspend the trial, a USM notification should be sent by the Sponsor to the MHRA Clinical Trials Unit within 3 days from the date the measures are taken (in accordance with Regulation 30), in addition to the serious breach notification to the MHRA Inspectorate.

   b. A serious breach is identified at an investigator site in Mexico, which is likely to affect to a significant degree the overall scientific value of the trial. Notify the MHRA of the serious breach (other concerned competent authorities may also need to be informed).

Please see Appendix I for a selection of notifications that have been received to date that may help Sponsors when deciding whether to submit a notification of a serious breach.

This is not an exhaustive list. Other types of serious breaches may occur and it is the responsibility as Sponsor to assess the information and ensure appropriate reporting.

It is also the responsibility of the Sponsor to take appropriate corrective and preventative actions in response to the serious breach, and to document these actions. Actions may also be taken by the MHRA, as described below.

F. Potential actions by the MHRA:

Upon receipt of a serious breach notification, the MHRA will log and review the notification, and a variety of actions may be taken, depending on the nature of the breach and its potential impact e.g.

- Acknowledgement of receipt, but no immediate action e.g. if appropriate action has already been taken by the sponsor. The case may be examined during future MHRA inspections.
- Request for additional information from and investigation by, the Sponsor. If insufficient information is provided in the initial notification to assess the impact of the breach, follow-up information will be requested.
- Sharing of information with other concerned parties, in accordance with the regulations and applicable agreements e.g. to concerned Ethics Committees, other competent authorities, MHRA Clinical Trials Unit.
- Investigation by the MHRA, for example, triggered inspection(s).
- Implementation of urgent safety measures, where appropriate.
- Suspension or termination of a clinical trial authorisation, where appropriate.
- Referral for enforcement action e.g. infringement notices, criminal investigation.
- Referral to professional bodies e.g. the General Medical Council.

G. References

- **Statutory instrument 2004/1031:** The Medicines for Human Use (Clinical Trials) Regulations 2004.
- **Statutory Instrument 2006/1928:** The Medicines for Human Use (Clinical Trials) Amendment Regulations 2006.

Appendix I

Notification Examples

Notified by:	**Issue:**	**Would MHRA have expected this case to be notified?**
Sponsor	Dosing error. Ethics Committee & MHRA informed. Subjects withdrawn. The sponsor stated that there were no serious consequences to subjects or data.	No, if there was no significant impact on the integrity of trial subjects or on scientific validity of the trial.
Sponsor	Patient Information Leaflet and Informed Consent updated. At one trial site this was not relayed to the patients until approximately 2-3 months after approval. *More information on the potential consequences of the delay should have been provided.*	Possibly not. If this was not a systematic or persistent problem and if no harm to trial subjects resulted from the delay. Yes, if there was a significant impact on the integrity of trial subjects.
Sponsor	Visit date deviation. *A common deviation in clinical trials.*	No. Minor protocol deviation, which does not meet the criteria for notification.
Contractor	Investigator failed to report a single SAE as defined in the protocol (re-training provided).	No, if it did not result in this or other trial subjects being put at risk, and if it was not a systematic or persistent problem. In some circumstances, failure to report a SUSAR could have a significant impact on trial

		subjects. Sufficient information should be provided for the impact to be assessed.
Identified during inspection prior to the current requirement to report serious breaches	Investigator site failed to reduce or stop trial medication, in response to certain laboratory parameters, as required by the protocol. This occurred with several patients over a one year period, despite identification by the monitor of the first two occasions. Patients were put at increased risk of thrombosis.	Yes, under the current requirements, this should have been reported as a serious breach.
Sponsor	Becomes aware of fraud at investigator site in the UK, which does not affect the overall scientific value of the Sponsor's trial or the integrity of trial subjects in the UK. However, the Sponsor is aware that the fraudster was involved in trials being sponsored by other organisations.	Although, in this situation, not a legal requirement under 29A, MHRA encourages voluntary reporting of all fraud cases in the UK, because MHRA will wish to establish the impact on the other trials in case subject integrity or the scientific value of those trials was compromised.

Appendix II

Notification of Serious Breach of Good Clinical Practice or the Trial Protocol to MHRA

(Ref: UK Statutory Instrument 2006:1928, Regulation 29A)

Your Name:	Your Organisation:
Your Contact Details:	Date Breach Identified by Sponsor:
Details of Individual or Organisation committing breach:	Details of related study (e.g. study title, EudraCT No) if applicable:
Please give details of the breach. Where possible, please include your rationale (e.g. patient safety / data integrity issue and relevant legislation if known). (continue on additional sheets if required)	

Please give details of action taken: (continue on additional sheets if required)

FOR MHRA USE ONLY:

Date Received:	GCP Ref Number:

Please forward this notification to GCP-PV.Inspectors@mhra.gsi.gov.uk OR GCP Inspectorate, MHRA, 18-103, Market Towers, 1 Nine Elms Lane, London, SW8 5NQ